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THE TUFTS POSTGRADUATE MEDICAL PROGRAM

SAMUEL PROGER, M.D.*

BOSTON

MOST postgraduate programs in operation today represent an attempt to continue the methods and technics of undergraduate instruction, making only what changes and modifications are required by the fact that the status of the practicing physician differs from that of the undergraduate. Much has been accomplished by this method, but perhaps more might be accomplished if the problem of postgraduate medical education were attacked not only from the standpoint of the school's relation to the practicing physician as a student, but also from the point of view of its relation to his hospital and his patients. Tufts College Medical School has attempted to do this.

In a sense, the problem of postgraduate medical education is the problem of the distribution of better medical care. Just as the fruitful attempt to solve the problem of undergraduate medical education has been largely responsible for the creation in this country of what are probably the world's highest medical standards, so conceivably could a comparably successful solution of the problem of postgraduate medical education assure the widespread utilization of the benefits of these high standards. Much vertical progress has been made, so that today American medicine, at least in its peaks, towers high. On the other hand, horizontal progress has been slow, and it must be admitted that our medical advances can be more widely, more rapidly and more effectively distributed.

Fundamentally, postgraduate medical education is, as the name implies, a union of the academic and clinical aspects of medicine. Logically, therefore, this union can best be maintained through an educational and clinical institution, that is, a medical-school and hospital center. During the last three years an attempt to develop such a fusion for the benefit of practicing physicians has been made by the New England Medical Center, which comprises Tufts College Medical School, the Boston Dispensary, the Boston Floating Hospital and the Joseph H. Pratt Diagnostic Hospital. This work, so far experimental in nature, has been made possible by the Bingham Associates Fund, of which Dr. George B. Farnsworth is president.

The program has operated through three types of hospitals: the medical-school and hospital center, hospitals in regional centers and small community hospitals. The teaching facilities of each type of hospital are integrated into a single program. The teaching does not emanate from the central source alone. Rather, an attempt has been made to decentralize all activities as much as possible, in the effort to develop every local academic potentiality. Hence, one type of teaching is conducted through the central institution, another through the hospitals in the regional centers, and still another through the small community hospitals.

We have thought of the hospital as an instrument for teaching, regardless of its size or location. As each hospital becomes more of an educational institution, the standard of medical practice within it of necessity rises. This has been a well-nigh universal experience in hospitals that have assumed academic functions. What has been done in the past by medical schools for relatively large hospitals conveniently located to the school, Tufts now hopes to do for hospitals of various sizes, widely separated and distant from the academic center.

There are three general divisions of the program, divisions that to a large extent are interdependent and complementary. They are the Diagnostic Hospital Service, hospital extension services and postgraduate medical courses. Analysis will reveal that these divisions fit into a coherent educational design.

DIAGNOSTIC HOSPITAL SERVICE

Those fortunate enough to be intimately associated with a teaching hospital are fully aware of the educational advantages of such an associa-

*Professor of clinical medicine, Tufts College Medical School; medical director, Joseph H. Pratt Diagnostic Hospital.

tion. Contact with the stimulating environment of an academic institution often creates in the physician an unconscious, sustained and effective stimulus to self-education. This constitutes what is probably the most satisfactory of all forms of postgraduate medical instruction. The fact that there are relatively so many well-informed physicians among those connected with teaching institutions is thus by no means purely accidental.

Through the Joseph H. Pratt Diagnostic Hospital and affiliated hospitals, we have attempted to make available to a large number of general practitioners in New England at least some of the educational advantages that derive from contacts with teaching institutions.

First in this regard may be mentioned the full medical reports that are submitted to the referring physicians. In this sense, all institutions, and their physicians as well, to which problem cases are referred may serve in a teaching capacity.

Secondly, in an effort to make these medical reports on referred cases as instructive as possible, we incorporate with the report on findings and recommendations sent to the referring physician a discussion of the clinical problems involved. With this abstract, when desirable, is a carefully selected bibliography; and whenever possible, reprints of the articles noted are sent on request. As an example, a general practitioner in a small town in New Hampshire referred to the Joseph H. Pratt Diagnostic Hospital for study a young woman who was suffering from a peculiar hardening of the skin. Our studies indicated that she had a condition known as scleredema adultorum of Buschke. The referring physician received, in addition to a full clinical report, the following:

> Apparently the best recent article dealing with Mrs. N.'s disease is one by Sweitzer and Laymon (*Archives of Dermatology and Syphilology* **37**:420, 1938), entitled "Scleredema Adultorum (Buschke)." The following sections from this article seem especially appropriate.
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> *Clinical Features.* Scleredema adultorum typically is characterized by induration involving the deep layers of the cutis, the subcutaneous tissues, the fascia and the muscles. The condition appears shortly after an acute infectious process, such as grippe, influenza, scarlet fever, measles, mumps or angina. It usually begins on the nape of the neck and spreads rapidly by continuity to the face, the shoulders, the arms, the back, the chest and the abdomen. In contrast to diffuse scleroderma, the hands and the feet are not affected. Although the cutaneous hardness is painless, the involved areas feel tense, and interference with mobility is not uncommon. Chewing, talking and the movements of respiration become difficult. The patient frequently states that he feels as though he were enclosed in a suit of armor. The smaller folds of the skin are lost, and when palpated the tissues feel as if they were permeated by paraffin. The induration is deep and extremely firm, and pitting like that associated with ordinary edema it is impossible to elicit. Important disturbances of sensation or sweating are not usually present. The skin is generally cool and pale, although erythematous patches or a livid hue have been noted.
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> The disease reaches its height within a few weeks, after which there is a stationary period of variable length. In practically all cases there is complete involution within eighteen months. Females are more frequently affected than males. Of sixteen patients whose cases were reviewed by Edmund Hoffmann, only five were males. The disease has occurred at various ages from infancy to middle adult life. Cases of so-called scleroderma in infants have been thought by some observers to be instances of scleredema.
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> *Diagnosis.* The first step in the diagnosis of scleredema adultorum is its differentiation from diffuse scleroderma, especially during the acute stages of both diseases. The facts that scleredema adultorum follows an acute infection, seems deeper in the cutis, lacks the characteristic ivory color of scleroderma and never presents pigmentation or atrophy are the most important aids in diagnosis. Scleroderma lacks any definite relation to infection and usually begins on the hands or the feet, while scleredema never involves those portions of the body. A period of observation may be necessary to establish the diagnosis as scleredema follows a more rapid course and, as a rule, regresses spontaneously, while diffuse scleroderma is slowly progressive.
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> *Therapy.* Since spontaneous involution generally occurs in scleredema adultorum, it is difficult to evaluate the various therapeutic measures which have been used. Sodium salicylate, thyroid and other glandular extracts have been administered internally, while warm baths, massage and the application of heat (diathermy) have apparently been of some value in causing a regression of the disease. Too favorable a prognosis should not be given, since it is impossible to predict exactly when the condition will subside.

As a further example, should a patient have epilepsy, the referring physician would receive, in addition to a complete clinical report, a full discussion, in abstract form, of epilepsy, as well as pertinent quotations from recent articles on the details of therapy, especially with regard to the use of Dilantin.

This type of instruction is wholly personal. Even the busy physician may be expected to read such material carefully, since it deals so specifically with a problem of immediate interest to him. He is thus given in concentrated form instruction concerning a clinical problem with which he is at the moment faced and about which he must do something. This problem has been of such concern to him that he makes the effort to send the patient who presents it to Boston, because he needs help. The referring physician is therefore given bedside instruction on his case comparable

to that which a clinical teacher in a hospital might give a house officer who, following a case work-up, desires advice and instruction. In this manner, the general practitioner in an isolated community may profit educationally from contact with a teaching institution.

A third educational feature consists in pertinent follow-up information. The hospital attempts to keep referring physicians informed of any important developments coming to its attention that may be of benefit to previously referred patients. For example, we have in the last several years seen a number of patients with parkinsonism. These patients were returned to their physicians with a recommendation for treatment by the more or less generally accepted method, with stramonium and scopolamine. Recent articles have appeared reporting good results in the treatment of parkinsonism with the use of the so-called "Bulgarian belladonna." An abstract describing this treatment was therefore sent to each of the physicians who had referred patients with Parkinson's disease. This abstract gave information about the drug and its use, with references to the published reports, for those who wished to obtain further details.

This type of critically filtered information has proved valuable, and it is our intention to extend its use still further, so that the practitioner in an outside community may come to feel almost as though he were on the active staff of the teaching institution.

Through the establishment of such an intimate relation between instruction and the actual care of patients, it is believed that Tufts College Medical School will inevitably increase the scope of its aid to its graduates, as well as to many other general practitioners.

A fourth educational feature of the Diagnostic Hospital Service is the *Bulletin*, which is published every other month and which contains clinical information derived from the various teaching activities at the New England Medical Center, particularly from the daily morning staff conferences at the Joseph H. Pratt Diagnostic Hospital. The *Bulletin* has an unusual appeal in that many of those physicians receiving it have been present at the morning conferences; and this familiarity, one may believe, is not only pleasantly reminiscent but is active in overcoming the customary lack of interest shown by medical men in material of this kind. To those who have attended the morning conferences as undergraduate or postgraduate students, the *Bulletin* represents an educational contact that makes continuous at least one important phase of a past educational experience.

In addition to the four educational features of the Joseph H. Pratt Diagnostic Hospital listed above, we hope, at a future date, to provide at the New England Medical Center living facilities for those physicians who, through their local community, are in one way or another affiliated with us. Their occasional visits to Boston will thus bring them directly into an academic atmosphere, which should serve as a helpful and pleasant stimulus to their medical interests.

With the anticipated completion of full clinical facilities at the New England Medical Center, the central hospital part of our teaching program can be expected to become much more inclusive, along the lines indicated above.

Hospital Extension Services

The hospital extension services are an important and at the same time unorthodox feature of our teaching program. These services are designed to make available improved hospital facilities for medical practice in the various communities concerned. It is clear that a postgraduate program that simply indicates to the general practitioner the value of improved laboratory, x-ray and electrocardiographic facilities, and then leaves him with no opportunity to avail himself of such aids, is not well rounded. A full educational program should take into consideration the hospital in which the physician practices, as well as the physician himself, and the possibilities for educational aid to those members of the hospital staff, nonmedical as well as medical, whose services are auxiliary but without which modern medicine cannot be satisfactorily practiced. Such considerations led to the development of the hospital extension services.

These services are co-ordinated through the medical-school and hospital center, the hospitals in the regional centers and the small affiliated hospitals. The small community hospitals have their direct affiliations only with the regional centers, the regional centers being in turn directly affiliated with Tufts College Medical School and the New England Medical Center. At present, regional centers are located in Lewiston (Central Maine General Hospital) and Bangor (Eastern Maine General Hospital). The small hospitals affiliated with the Central Maine General are in Brunswick, Rockland, Bath, Damariscotta, Camden, Skowhegan, Waterville, Augusta, Farmington, Rumford and Boothbay Harbor. Those affiliated with the Eastern Maine General are in Greenville, Dover-Foxcroft, Belfast, Blue Hill, Cas-

tine, Bar Harbor, Machias, Lubec, Calais, Island Falls and Houlton. The plan of working with small hospitals through intermediary centers has proved most satisfactory, as indicated in a previous paper on the subject.*

Services are now being offered in the fields of pathology, electrocardiography, radiology, laboratory aid, dietetics and library assistance. Briefly, these functions are as follows:

Pathology. Since pathology is a highly specialized subject, it is impracticable for physicians to practice part-time pathology as they may, for example, practice radiology. As a result, the small community hospital usually has no local pathologist. Under hospital extension services, all tissue specimens are routinely sent from the small hospitals to the regional-center hospital. An immediate report is sent back, by telephone when necessary, and all questionable specimens are sent on to the head of the Pathology Department at Tufts College Medical School, who is at all times available for consultation. On request, the pathologist in the regional center will gladly review all slides with the interested physician. In an increasing number of cases, furthermore, post-mortem examinations at the affiliated hospitals have been performed by the regional-center pathologist; this is a valuable indication of growing interest on the part of local practitioners. The regional-center pathologist is also available for clinicopathological conferences in the small communities.

Electrocardiography. A course of one week's duration in the interpretation of electrocardiograms is given to representatives of the community hospitals. The course is given without charge on the condition that the hospital purchase an electrocardiograph. Then, from the community hospitals, the local electrocardiographer sends a copy of every tracing to the electrocardiographer in the regional center, whose reports become available for check by the physicians in the community hospitals. The tracings that are unusually difficult to interpret are sent from the regional center to Boston, where several well-known cardiologists are available when necessary. In this manner, the small hospitals have available the best authorities on the interpretation of electrocardiograms, when they are needed. At the same time, the electrocardiographer at the small hospital is given constant opportunity for supervision and improvement.

The short course in electrocardiography thus serves as the beginning of a continued and permanent form of instruction. This principle is at once one of the most distinctive and most important features of our teaching efforts. Some of the other specialized courses recently given, such as in allergy and hematology, as well as to a large extent the regular courses in general medicine, pediatrics, obstetrics and gynecology, may all be taken as similar examples. This arrangement for postgraduate courses appears to have definite advantages over the customary method of simply offering, to whoever wants it, a course when he wants it. A course that is only an isolated cross-sectional experience in a physician's life is not likely to mean so much to him as one that is a regular part of his active professional career.

Roentgenology. Through a recently inaugurated plan, x-ray seminars are held every two weeks at the Eastern Maine General Hospital in Bangor. These are attended by the roentgenologists from the affiliated community hospitals, and traveling expenses are covered by the Bingham Associates Fund. All routine films are sent in advance to the regional hospital, so that consultation notes concerning them will have been dictated and the films of particular interest will have been chosen for discussion at the seminar. Thus, when the men meet, there is discussion of the problems with which they are immediately concerned, and of the general x-ray problems with which they should be kept familiar. This program serves not only as instruction to the doctor but also as a consultation service to the patient, a feature that is likewise significant in the pathological and electrocardiographic services. In addition, it has the advantage of giving the radiologist an opportunity to profit from the experience and material of ten hospitals instead of being limited to his own. In the interval between the seminars, emergency films may be sent in for examination, and the Bangor roentgenologist also makes occasional visits to the local hospitals to help them and to become acquainted with their equipment and facilities. The Bingham Associates Fund makes it possible for the regional radiologist to attend the weekly radiologic seminars at the Massachusetts General Hospital in Boston, which thus becomes, when necessary, a final court of appeal for the small hospitals, serving at the same time as a valuable source of instruction and education to the regional radiologist. The x-ray technicians in the small hospitals meet every second month at the Eastern Maine General Hospital in Bangor for a conference on their own problems. Fellowships for further study in Boston are available for them when needed.

In the Lewiston group, the regional radiologist visits the affiliated hospitals once a week, the pro-

*Proger, S. The Joseph H. Pratt Diagnostic Hospital. *New Eng. J. Med.* 220:771-779, 1939.

gram otherwise being essentially the same as that of the Bangor group. Of the two, the Bangor plan seems to be more promising, since it is capable of reaching an unlimited number of hospitals in a large area, and geographical factors are minimized.

Laboratory aid. Scholarships are granted to x-ray and laboratory technicians for advanced and specialized studies, chiefly in the laboratories of the Joseph H. Pratt Diagnostic Hospital. Technicians in each small hospital annually spend one month in Boston for the purpose of improving their technic and learning new methods and procedures. An itinerant technician is provided to substitute in the affiliated hospital for the duration of the course. During the fiscal year 1939–1940, twenty-seven such scholarships for technicians were awarded.

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Last winter, in addition, a one-week course in chemistry was given by the chief chemist of the Joseph H. Pratt Diagnostic Hospital at the Central Maine General Hospital for the technicians of the Lewiston group. Attendance at its sessions was large, and demonstrations, appraisals and criticisms of methods were carried out.

In an attempt to standardize laboratory procedures, many of the hospital laboratories receive from the central laboratories solutions of the various reagents used in tests. By means of this arrangement, the number of variable factors is reduced, and accurate results are more easily obtainable in the small community hospitals.

Some of the affiliated hospitals are so small (10 to 20 beds) that they do not seem to require a full-time laboratory technician. No hospital is too small to have nurses, however, and we have therefore arranged for hospitals in this category to send one of their graduate nurses to Boston for a three-month period of instruction in the technic of performing a certain number of simple but important laboratory tests. Through such a course, and annual one-month courses thereafter, it is possible for a graduate nurse to perform, on a part-time basis, common laboratory tests in a small community. Arrangements have been made for the more difficult tests to be done in the regional centers.

Dietetics. In dietetics, postgraduate study is made possible largely through scholarships, which enable the dietitians in the community hospitals to spend one month of each year regularly at the New England Medical Center, where they are given a continued course of instruction, through which they are kept informed of progress in their field.

Library assistance. The Gerrish Library at the Central Maine General Hospital serves as a central library for the entire Lewiston group. It prepares bibliographies and sends out books for practitioners, as well as conducting a mailing service on current journals. The affiliated hospitals regularly receive selected current journals by this system. After four days, the journals are sent on to the next hospital, and new ones are received. The plan has received enthusiastic co-operation among the participating hospitals, and many libraries may well envy their record of not one journal lost during the year, although most of the journals have been consulted by many staff doctors.

In addition to these services now being offered, it is hoped that aid may in the future be given in the fields of nursing, anesthesiology and hospital administration.

In summary, then, it is clear that through a system of scholarships and direct hospital consultations a practicable method of continued education in certain auxiliary medical fields has been established. In pathology, instruction is given in the form of consultations and supervision of technical and diagnostic work by the professor of pathology at Tufts College Medical School. In roentgenology, the instruction involves supervision and consultation work by the roentgenologists in the regional centers, who in turn are enabled through a fellowship to attend the weekly seminars at the Massachusetts General Hospital. In laboratory work, the instruction is through annual scholarships for one month's actively supervised work at the New England Medical Center. A similar arrangement obtains in dietetics. In electrocardiography, the instruction in the small communities consists of routine consultations on all tracings, whereas for the electrocardiographer in the regional center, instruction through consultation is available when necessary. In general, it is evident that there is opportunity for a free and automatic exchange of opinions between small communities, regional centers and the metropolitan teaching center.

Teaching Ward Rounds

Another feature of the extension service is aimed directly at the staff members of the affiliated hospitals, namely, teaching ward rounds. It is our belief that the best sort of extramural clinical teaching we can offer practicing physicians is such instruction as may be given through actual contacts with patients, as on ward rounds. Apparently the most satisfactory sort of instruction in general medicine that graduates obtain in their internships is that which they receive from the more or less informal discussions incident to ward rounds and directly related to cases and clinical

problems with which they have intimate association. Since this type of instruction has proved universally effective, it has seemed desirable to apply it in our own work. This we have done, with most encouraging results, by having instructors, chiefly members of our own staff, conduct teaching rounds once a month in the affiliated hospitals. In this manner, we are able to present an informal type of regular instruction that, it is fair to presume, offers much of value, if for no other reason than that it deals with timely and important local problems with which the local men are familiar. An informal discussion by a qualified instructor, in the course of such rounds, on how to treat John Smith (whom most of the local doctors know), who has a bleeding duodenal ulcer, is likely to produce a much stronger impact from the educational point of view than a formal discussion by the same instructor to the same group on the treatment of peptic ulcer.

Correspondence follow-up is applied to this ward-round instruction. The instructor who conducts the rounds sends, within the four weeks following his visit, an informal letter to each of the staff members of the community hospital, presenting some of the recent literature concerning the cases seen on rounds, offering critical comments, and summing up the most important points raised during the visit. In this manner, many of the case discussions on ward rounds are followed up by written instructions. With a different instructor to conduct teaching rounds each month, the staff members of the hospitals concerned receive written or oral instruction almost every other week throughout an academic year (eight or nine months), whereas the individual instructors are not too greatly burdened.

Some of the advantages of instruction through teaching ward rounds are as follows. A natural consequence of the meetings is that the local physicians whose cases are presented are stimulated to improve the quality of their case work-ups. References made to desirable procedures, facilities for which are lacking, in diagnosing or treating the cases under discussion occasionally prompt the staff and hospital to provide for such procedures in the future, thereby improving the entire local apparatus for diagnosis and treatment. A large number of our teaching staff are given an opportunity for intimate contact with most of the staff members of the affiliated hospitals, resulting in a wide diffusion of men and ideas. We are able further to utilize in our teaching program our hospital affiliations. We have the opportunity to offer instruction through what is generally considered the best possible medium, namely, a small community hospital. We reach most of the physicians in the hospitals concerned. The effectiveness of this instruction is prolonged through the correspondence follow-up.

Postgraduate Courses

These courses consist essentially of more or less orthodox short courses in various medical and surgical fields. They vary in duration from one to four weeks and are especially designed for general practitioners. Almost all the courses are given at the New England Medical Center.

Until 1940, only one-month courses were given. There are many reasons why courses of less than one month's duration are undesirable. In fact, even one month is not really long enough for truly adequate instruction in such fields as general medicine, pediatrics, obstetrics and gynecology. However, the more serious objections are avoided if these shorter courses are intended not to serve as complete instruction in any field, regardless of how limited that field, but rather as the beginning of continued instruction.

The advantages of longer periods of instruction are obvious. There are certain real disadvantages. First and foremost is the fact that such courses (one month or more) are at best taken by a relatively small number of physicians in a given area (about 10 per cent, in our own experience as well as in that of others). If by the nature of things only about 10 per cent of the physicians are reached by a given program, the program is automatically limited in its usefulness.

One month is longer than most physicians feel they can safely spend away from their practices. The fact that they can safely spend a month away is not nearly so important as the fact that 90 per cent of the physicians do not believe that they can, or have no desire to devote a month to additional training. The shorter courses would meet the objections at least of some of those who find a month too long.

The principal reasons, then, for instituting one-week courses, after having for three years given only those of one month's duration, may be outlined as follows. A greater number of men may be expected to leave their practices for one week than for one month. In a limited subject, much more concentrated and effective teaching can be given. The students are apt to be more interested in the instruction, since it will be directed toward a subject that they themselves have selected rather than one that covers a general field, many aspects of which may not be of particular interest to them. Experiences throughout the country have indicated that short, intensive courses are, by and

large, more satisfactory than longer ones. The subsequent correspondence, as outlined below, prolongs the effectiveness of such a course.

The courses themselves are, as mentioned above, essentially no different from those given in many schools throughout the country. Two features associated with this part of our teaching program, however, are not widespread and hence deserve some special mention. First, living quarters in the institution are provided for those taking courses. Our efforts have always been directed toward making the postgraduate student throughout his stay with us, and thereafter, if he wishes, an integral part of our organization. The fact that most of these students live with us during their course of study — and will be enabled to do so, we hope, on their repeated visits to Boston subsequently — has tended even further to integrate their work with that of the institution. Throughout their stay, they are constantly in a medical atmosphere, and live and mingle freely with residents, visiting staff and fellow students. This has proved of real value.

The second distinctive feature of this part of our program is the follow-up procedure, whereby physicians who have participated in a course are kept informed by letters from their instructors of new developments in the field covered by the course. These letters are sent out as new material of value to the practicing physician appears in the current literature to which he may not have access, or as new experiences develop that the instructors deem worthy of transmission to the physicians who have participated in their courses.

Discussion

In formulating plans for a postgraduate medical program, it may be helpful critically to analyze past programs, many of which, although magnificent in conception, failed to achieve their aims. In these unsuccessful efforts, at least one fact stands out as a possible cause of ultimate failure, namely, that for success they were dependent on the voluntary and active co-operation of the practicing physicians. Widespread voluntary co-operation can be stimulated temporarily by an intensive campaign or it can be maintained locally by a forceful personality, but it cannot be ingrained, so that sooner or later the initial force subsides, interest wanes, and the program collapses.

Any program, therefore, to be successful on a broad scale must be directed toward the development of a condition in which continual education will be automatic, regular and taken for granted. In other words, active interest and co-operation on the part of the student physician will not be a prerequisite to initial work, but passive acquiescence alone will be necessary. Perhaps it is not too much to say that the majority of physicians are not interested in continued education when such education requires any undue application or even slight sacrifice. Indifference under such circumstances is unfortunately a widely prevalent human trait, and any program that presumes that higher motives can be made to prevail generally is doomed to failure.

Perhaps this point will indicate, on the other hand, at least some of the factors responsible for the comparatively wide success of undergraduate education. It appears that a fundamental condition in successful educational programs, such as undergraduate programs, is that, to acquire various benefits, certain requirements must be met by the student; and these demand consideration. Study is not made an end in itself, but rather a means to an end, to a definite and to a practically desirable end. Undergraduate educational programs assume that an altruistic goal is not capable of stimulating sustained effort or interest. Hence, we have diplomas, credits, degrees and so forth. These are but artificial and arbitrary goals set up to serve as prolonged stimuli for the production of sustained effort. Students work for four years toward a degree much more conscientiously than they study for enlightenment; they "work for a degree." Some such stimulating force is necessary to overcome normal human inertia, and to be permanently effective it must be permanently active. Why, if artificial stimulation is required for effective undergraduate education, should we assume that the field of postgraduate education can do without it? Actually, there is reason to believe that in older age groups some means is even more necessary for overcoming the human tendency to do nothing that is not required for an obvious and immediately desirable end. Those in the older groups at least have their time otherwise fully occupied.

What we have done has tended to make our teaching program so much a part of a physician's daily life that to some extent it has become automatic and continuous. We have thus far done little in the way of direct inducements. This we hope to do through plans now being developed for more direct affiliations between practicing physicians and the medical school, through the local hospitals, and also through regular opportunities for academic and professional recognition.

Summary

The members of the faculty of Tufts College Medical School look on the problem of postgrad-

uate medical education as intimately bound up with the problem of the distribution of better medical care. They have therefore developed a postgraduate medical program that goes beyond the traditional relation of teaching institution to physician, to extend to that physician's hospital and to his patients as well. Thus, although the program includes postgraduate courses for practicing physicians, it is also concerned with improved hospital facilities, as well as diagnostic services, for those physicians, and through them for their patients.

The program functions through the medical school and affiliated hospitals of various sizes (small community hospitals, larger hospitals in regional centers, and the central, medical school and hospital center). What has been done in the past by medical schools for relatively large hospitals conveniently located to the school, it is now hoped can be done for hospitals of various sizes, widely separated and distant from an academic center.

The program is divided into three parts: the Diagnostic Hospital Service, hospital extension services and postgraduate medical courses. In general, the attempt has been made to offer the medical student continued contact with his school throughout his medical career, through the medium of his local hospital and his patients, as well as through the customary postgraduate courses.

The program is so designed as not to interfere with existing educational activities, such as teaching clinics, community and other society meetings, staff meetings, medical-journal reading and so forth; it is intended rather to stimulate and supplement such activities.

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CHLOROSIS*

ISADORE OLEF, M.D.†

BOSTON

CHLOROSIS, defined by Patek and Heath[1] as "a hypochromic anemia in adolescent girls and young women, usually associated with gastrointestinal and menstrual disturbances," is considered today a medical curiosity. In view of its frequency during the latter part of the nineteenth century and its rapid regression since then, "chlorosis seems destined to occupy only a niche in medical history rather than the prominent place among blood dyscrasias which it has held in the past."[2] It is extremely unlikely, however, that a disease etiologically dependent on universally current conditions such as growth, blood loss and inadequate diet should completely disappear. There is no doubt that chlorosis was quite frequent half a century ago. Its high incidence then, however, was more apparent than real. This is obvious from von Hoesslin's[3] critical analysis of 143 cases diagnosed as chlorosis. Of these, 64 had histories suggesting tuberculosis; 25, gastric ulcer; 13, psychoneurosis; 13, secondary anemia due to endocarditis or other infections; and 5, excessive blood loss. The remaining 23 cases might have been called "possible chlorosis." It is true, on the other hand, that chlorosis in severe form is rather uncommon at the present time. One of the factors responsible for the apparent rarity of the disease today is the allocation of many mild and some severe cases of chlorosis into the categories of nutritional anemia or microcytic anemia with achlorhydria. Among Mills's[4] cases of idiopathic hypochromemia, for example, one twenty-six-year-old patient had been anemic for ten years. In McCann and Dye's[5] series of cases of chlorotic anemia with achlorhydria, one nineteen-year-old woman had been anemic for five years. These were probably cases of adolescent chlorosis.

Chlorosis, therefore, is not so rare today as has been implied. During the last four years, I have personally observed 8 cases. Three of these (Cases 1, 2 and 3) have been reported.[6] There was no clinical or laboratory evidence in any of these patients of acute, recurrent or chronic infections, severe visceral disease or abnormal blood loss.

CASE REPORTS

CASE 1. A 19-year-old girl was seen in November, 1936, complaining of weakness, some shortness of breath, palpitation and vague pains in the lower abdomen. Born in Scotland, she had come to the United States at the age of 2 years. She was born at term and was of normal weight at birth. She received neither orange juice nor cod-liver oil during early infancy. Her appetite had always been capricious, and her diet grossly deficient in green vegetables and meats. At the age of 5, she was told that she was anemic and was given some medicine for the anemia; this she took for a short time. At the age of 10, she was told again by a physician that she was anemic; this time she took the prescribed medicine for about a month. Her

*From the Medical Clinic, New England Medical Center, and the Department of Medicine, Tufts College Medical School. This study was aided by grants from the Charlton Research Fund, Tufts College Medical School, and the Bingham Associates Fund.

†Associate physician, New England Medical Center; assistant professor of medicine, Tufts College Medical School.

menses had begun at the age of 14 and had always been very scanty, particularly during the previous year.

There was no history of any previous serious illnesses or operations.

On examination, the patient appeared well developed and plump. She had a temperature of 100°F. by mouth. The skin was strikingly white, with a suggestion of a greenish tint. The face was definitely puffy. The scleras were not icteric. The mucous membranes of the mouth were very pale. The tongue appeared normal. The heart was normal except for a soft systolic murmur over the mitral area. Examination of the lungs, abdomen, pelvis and rectum was negative. The extremities were negative except for some pretibial pitting edema. The fingernails appeared rather thin.

The urine and stools were normal. The blood Hinton reaction was negative. The other initial laboratory findings are presented in Table 1, and the results of the gastric analysis are shown in Table 2.

The patient was given 4 gr. ferrous sulfate thrice daily. At the end of 7 weeks the red-cell count was 4,700,000, and the hemoglobin 82 per cent (Sahli).

The patient felt fairly well for nearly 2 years. The duration and quantity of her menses had remained essentially normal during this period. She was seen again in September, 1938, complaining of fatigue. Physical examination was essentially negative. The urine and stools were normal. The laboratory findings are shown in Table 1, and the results of the gastric analysis in Table 2. The patient was again placed on ferrous sulfate therapy, 4 gr. thrice daily. At the end of 6 weeks, the red-cell count was 4,250,000, and the hemoglobin 82 per cent (Sahli).

Case 2. A 19-year-old girl was first seen by Dr. Frank Mirabello in November, 1936, when she complained of a mild "head cold." She was born in Nova Scotia and had been in the United States for 3 years. She was born at term and had normal weight at birth. Her diet had always been adequate. Menstruation began at the age of 13, and the quantity, duration and recurrence of the menses had apparently been normal.

On examination, the patient appeared well developed, but rather thin. There was slight swelling and reddening of the mucous membranes of the nose, and some generalized injection of the throat. The temperature was normal. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. The heart, lungs, abdomen and extremities were normal, as were the fingernails.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings are given in Table 1, and the results of the gastric analysis are shown in Table 2.

The patient was placed on 4 gr. ferrous sulfate therapy thrice daily. At the end of 5 weeks, the red-cell count was 5,330,000, and the hemoglobin 82 per cent (Sahli).

Case 3. This patient, a twin sister of the patient in Case 2, presented a history identical with that given by her sister. She was seen first by Dr. Mirabello in November, 1936, when she complained of a mild upper respiratory infection. On examination, the patient appeared well developed and well nourished. There was slight swelling of the nasal mucous membrane, and slight reddening of the throat. The temperature was normal. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. Examination of the heart, lungs, abdomen and extremities was negative. The fingernails were normal.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings and the results of the gastric analysis are presented in Tables 1 and 2.

Under ferrous sulfate therapy, in doses of 4 gr. thrice daily, the red-cell count rose at the end of 5 weeks to 5,400,000, and the hemoglobin to 74 per cent (Sahli).

Case 4. A 19-year-old American-born Jewish girl was seen in March, 1939, complaining of scanty menstruation. She was born at term and was of normal weight at birth. The past history was not significant. The diet had always been adequate. Menstruation began at the age of 14 and remained regular for 1 year. During the previous 3 years, the menses had been intermittently scanty, more particu-

Table 1. *Initial Laboratory Findings in 8 Cases of Chlorosis.**

Case No.	Hemoglobin	Red-Cell Count	White-Cell Count	Platelet Count	Mean Corp. Volume	Mean Corp. Diameter	Polymorphonuclears	Lymphocytes	Monocytes	Eosinophils	Total Protein	Albumin	Globulin	Icteric Index	Sedimentation Rate
	%	$\times 10^6$	$\times 10^3$	$\times 10^4$	*cu. microns*	*microns*	%	%	%	%	*gm./100 cc.*	*gm./100 cc.*	*gm./100 cc.*		*mm./hr.*
1 (1936)	52	4.92	10.8	267	67	7.1	69	16	11	4	5.6	3.1	2.5	5	10
(1938)	71	4.58	8.8	70	—	—	58	33	7	2	—	—	—	—	8
2	55	4.44	7.5	50	—	6.7	58	35	5	2	4.7	2.7	2.0	5	9
3	50	4.16	6.3	147	—	6.7	55	37	6	2	6.3	3.1	3.2	5	8
4	56	3.84	5.1	41	—	—	58	32	8	2	—	—	—	6	6
5	68	3.94	7.0	54	—	7.0	55	40	2	3	6.5	4.3	2.2	9	4
6	56	3.94	5.6	48	—	7.0	55	35	9	1	8.1	5.3	2.9	8	8
7	57	4.83	7.1	50	—	—	54	**34**	**6**	**2**	—	—	—	—	18
8	28	3.30	7.2	117	67	—	81	**12**	7	0	—	—	—	—	8

*The stained blood films of all these cases revealed small, pale red cells showing moderate anisocytosis and poikilocytosis. The films of Case 6 presented, in addition, some rouleaux formation.

Table 2. *Results of Gastric Analysis in Patients with Chlorosis.*

Case No.	Fasting		One Hour after Test Meal		One Hour after Histamine Injection	
	units of acid		units of acid		units of acid	
	Free	*Total*	*Free*	*Total*	*Free*	*Total*
1 (1936)	0	10	–	—	10	15
(1938)	0	10	–	—	0	10
2*	0	10	0	10	—	—
3	0	10	–	—	0	10
4	0	10	–	—	0	15
5	0	10	–	—	0	10
6*	0	10	0	10	0	30
7*	0	5	0	5	45	55
8	0	15	–	—	12	35

*Given a caffeine test meal.

larly during the previous 3 months. For the previous few weeks, the patient had had intermittent headaches. Three years previously, she was treated for a short time with iron for "secondary" anemia.

On examination, the patient appeared well developed, but rather thin. The scleras were not icteric. Examination of the eye grounds was negative. The mucous membranes of the mouth were pale. The tongue appeared normal. Examination of the heart, lungs and abdomen was negative. The fingernails were normal.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings and the results of the gastric analysis are presented in Tables 1 and 2.

The patient was given ferrous sulfate, in doses of 4 gr. thrice daily. At the end of 3 weeks, the red-cell count was 4,050,000, and the hemoglobin 82 per cent (Sahli).

CASE 5. A 14-year-old girl was seen in November, 1938, complaining of cramps in one hand. Her parents were Irish. She was born at term and had normal weight at birth. The past history was not significant. Her appetite had always been capricious, and her diet deficient for years in meats and green vegetables. Catamenia began at the age of 14 and had always been irregular and scanty. One year previously, the patient had been treated for a short time with iron for "nutritional anemia."

On examination, the patient appeared fairly well developed but rather thin. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. Examination of the heart, lungs, abdomen and extremities was negative. The fingernails were normal.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings are presented in Table 1, and the results of the gastric analysis are shown in Table 2.

At the end of one month's treatment with ferrous sulfate, in doses of 4 gr. thrice daily, the red-cell count was 4,590,000, and the hemoglobin 80 per cent (Sahli).

CASE 6. A 17-year-old girl was seen in August, 1938, complaining of a sore throat and pain in one knee of 2 days' duration. Her parents were Irish. She was born at term and had normal weight at birth. Her diet had been inadequate for several years in meats and green vegetables. Catamenia began at the age of 12, and the quantity, duration and frequency of the menses had apparently been normal.

The patient had had measles, pertussis, mumps and varicella. She had catarrhal jaundice at the age of 11. She was said to have had rheumatic fever at the age of 4, when she was in bed for 1 week.

Physical examination revealed a well-developed, pale girl. There was a definite greenish tint to the skin. She had an oral temperature of 100.2°F. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. There was mild generalized injection of the pharynx. The lungs were clear. The heart was normal in size; there was a short systolic mitral murmur. The rest of the examination, including that of the joints, was negative.

Examination of the urine was negative. Examination of the stools revealed a slightly positive reaction with the benzidine reagent on two occasions, but negative reactions on subsequent examinations. Woldman's[7] phenolphthalein test for enteric lesions was negative. X-ray examination of the chest was negative. Electrocardiograms revealed inverted P waves in Leads 2, 3 and 4, a finding that was suggestive of rheumatic heart disease but not of any acute involvement. The blood Hinton reaction was negative. The remaining initial laboratory findings are shown in Table 1, and the results of the gastric analysis are given in Table 2.

The temperature became normal in a few days and remained so.

In this patient, a therapeutic trial with arsenic was made initially—formerly, arsenic was a popular remedy for the treatment of various anemias; its mode of action, however, still remains obscure. Its effects in this patient were disappointing, as shown in Figure 1. Following the administration of Fowler's solution in gradually increasing therapeutic doses, there was a decrease in the hemoglobin, erythrocyte and platelet values. The most impressive change occurred in the total thrombocyte count, which diminished in a short time almost to the critical level. The subsequent administration of iron, however, in the form of 4 gr. ferrous sulfate thrice daily, produced a satisfactory remission. At the end of 6 weeks, the red-cell count was 4,500,000, and the hemoglobin 85 per cent (Sahli).

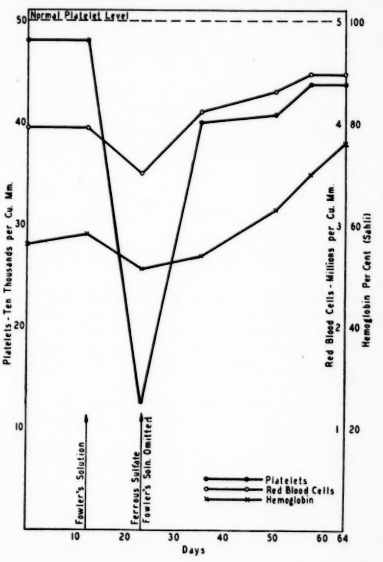

FIGURE 1. *The Behavior of the Hemoglobin and the Erythrocyte and Platelet Counts in Case 6 under Arsenic and Iron Therapy.*

CASE 7. A 22-year-old girl was seen in September, 1940, complaining of weakness, dizziness and anorexia of 1 year's duration. Her parents were born in the United States. She was born at term and had normal weight at birth. Her diet had been adequate. Catamenia began at the age of 14 and remained regular until 1 year before examination, when they became somewhat more frequent. There had been no change in the quantity of the menstrual flow. The past history was not significant.

On examination, the patient appeared well developed and well nourished. The mucous membranes of the mouth were pale. The tongue was rather small and slightly atrophic. Examination of the heart, lungs, abdomen and extremities was negative. The fingernails were normal.

Examination of the urine revealed the slightest possible trace of albumin on one occasion. Renal-function tests were negative, and the stools were normal. The blood Hinton reaction was negative. X-ray study of the chest was negative. The remaining initial laboratory findings are presented in Table 1, and the results of the gastric analysis are shown in Table 2.

The patient was given 4 gr. ferrous sulfate thrice daily. At the end of 8 weeks, the red-cell count was 4,800,000, and the hemoglobin 87 per cent (Sahli).

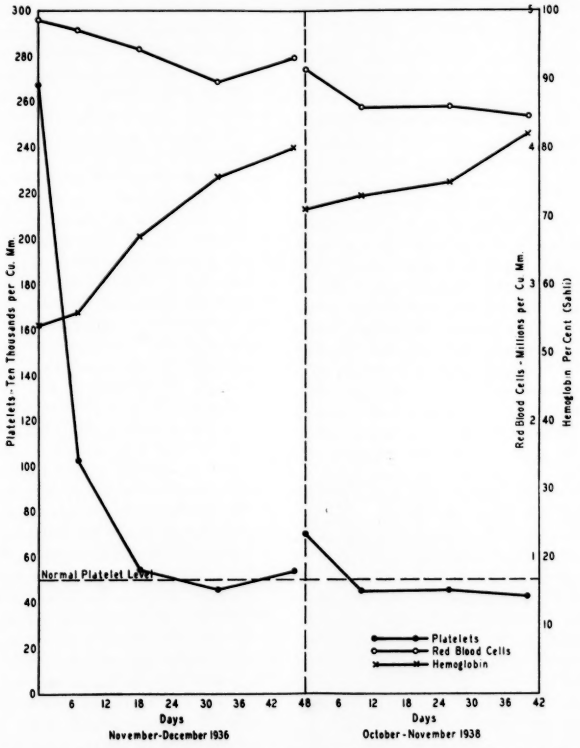

FIGURE 2. *The Behavior of the Hemoglobin and the Erythrocyte and Platelet Counts in Case 1 under Iron Therapy.*

CASE 8. A 16-year-old boy was seen in October, 1940. He had no complaints, and was referred by his school physician for observation because of unexplained anemia. His parents were of French-Canadian origin. He was born at term and was of normal weight at birth. His diet had been adequate. There was no history of any serious illnesses in the past.

Physical examination revealed a very well-developed and well-nourished boy. He had an oral temperature of 100°F. There was a definite greenish tint to the skin, and a marked pallor of the mucous membranes of the mouth. The tongue was rather large and smooth. There was a loud systolic murmur over the mitral and pulmonic areas. The fingernails were thin, brittle, flattened and spooned.

The first urine examination showed a very slight trace of albumin, but subsequent examinations were negative. The first stool examination showed a slightly positive reaction with benzidine reagent, but subsequent examinations were negative. X-ray studies of the chest and the gastrointestinal tract were negative. Electrocardiograms

were normal. The blood Hinton reaction was negative. Gastroscopy performed by Dr. Henry H. Lerner revealed evidence of acute and chronic gastritis. The other initial laboratory findings are shown in Table 1, and the results of the gastric analysis are presented in Table 2.

The patient was given 4 gr. ferrous sulfate four times daily. This was increased at the end of a week to six doses a day. At the end of 8 weeks, the red-cell count was 4,945,000, and the hemoglobin 85 per cent (Sahli).

Discussion

The anemia of patients with chlorosis is of the hypochromic microcytic type. The erythrocytes are flattened, small in size and poor in hemoglobin. An important and striking hematologic feature is thrombocytosis, which is not frequent, but which, when encountered, may be very marked. When thrombocytosis is present, the platelets undergo unusual quantitative changes after the institution of iron therapy. This behavior of the platelets is unique and very different from their behavior in other types of anemia under treatment, as I have pointed out elsewhere.[8] This is illustrated by Figure 2, which presents the hemoglobin levels and erythrocyte and platelet counts in Case 1. In November, 1936, the initial platelet count was 2,671,000 (normal count about 500,000[8]). Under iron therapy, the total thrombocyte count dropped promptly to approximately the normal level as the hemoglobin became elevated. Medication was discontinued at the end of about two months. When the patient was seen again in September, 1938, the platelet count was 700,000, and the hemoglobin 71 per cent (Sahli). The patient was obviously in mild relapse. Under iron medication, the platelet count again decreased to about the normal level as the hemoglobin values became elevated. The behavior of the thrombocytes in 1938, when the patient was in relapse, was the same, though not so spectacular, as in 1936. This inverse relation of the platelet values and hemoglobin levels represents an unusual hematologic finding. These quantitative changes in the platelets undoubtedly play a significant role in the development of the spontaneous venous thrombosis that is, at times, observed in these patients.

Gastric Acidity

Textbooks of medicine describe chlorosis as an anemia usually associated with either normal or increased acidity of the gastric contents. Many investigators, Naegeli[9] and Witts[10] among others, differentiate chlorosis from primary hypochromic anemia on the basis of the degree of the gastric acidity: in chlorosis, there is said to be an abundance of acid secretion in the stomach, and in primary hypochromic anemia there is usually anacidity. In the literature, however, one finds an array of most conflicting reports describing isosecretory, hypersecretory and hyposecretory types. The most comprehensive report is that of Arneth,[11] who examined the gastric contents of 23 patients with chlorosis and found the total acid levels to be either normal or increased. However, careful analysis of the cases reported by this author reveals that the diagnosis of chlorosis can be seriously questioned in a number of cases. At least 5 of the patients had diseases that by themselves could produce anemia or could easily aggravate considerably a pre-existing anemia. Arneth's levels for the total acidity after a test meal ranged between 0.15 and 0.25 per cent in normal persons, and between 0.15 and 0.38 per cent in patients with chlorosis. At the present time, the normal ranges for gastric acidity are given as 0.4 to 0.5 per cent for free hydrochloric acid, and 0.4 to 0.6 per cent for the total acidity (Levinson and MacFate,[12] Wright[13] and Müller and Seifert[14]). Despite the fact that Arneth employed laboratory methods quite similar to those used now, the results he obtained were certainly low when compared with present standards. Considered from this angle, all his patients had hypochlorhydria. Furthermore, Arneth determined only the total acidity. In analyzing the gastric contents, it is essential to determine both free and total acidity. Decrease or absence of free hydrochloric acid is usually associated with a decrease in the total acidity and is indicative of either functional or organic disease of the parietal or oxyntic cells in the stomach. This type of deficiency assumes considerable significance in certain types of anemia, more particularly in pernicious anemia, primary hypochromic anemia, nutritional anemia in children and chlorosis.

Patek and Heath[1] were the first to carry out gastric analyses with histamine on patients with chlorosis. Of the 4 cases they reported, 1 patient had normal gastric acidity, 1 had marked hypochlorhydria, and 2 had complete achlorhydria. In other words, 50 per cent of their patients had complete histamine achlorhydria, and 25 per cent histamine hypochlorhydria. Of the 8 cases herein reported (Table 2), 4 had total histamine achlorhydria, 2 had hypochlorhydria after the injection of histamine, 1 had achlorhydria after a test meal, and 1 had hypochlorhydria after a test meal and normal acidity after the injection of histamine. In this latter group, therefore, 50 per cent of the patients had complete histamine anacidity, and 25 per cent had histamine hypoacidity.

The frequency of true histamine anacidity in normal adults is 10.8 per cent (Bloomfield and

Polland[15]). A review of the literature discloses that achlorhydria, even after the injection of histamine, is rather common among the very young (Klumpp and Neale,[16] Neale,[17] Vanzant et al.[18] and Cutter[19]), then decreases rapidly in frequency, and remains low in incidence until about the age of twenty years. Between the ages of fifteen and twenty the incidence is very low (Vanzant et al.,[18] 2.8 per cent; Wright,[20] 1.2 per cent; Bockus et al.,[21] none; Polland and Bloomfield,[22] none). In other words, during the age periods when chlorosis is usually encountered, achlorhydria is rare. Therefore, the high incidence of histamine hypochlorhydria and achlorhydria found in patients with chlorosis must be considered one of the most characteristic features of this disease.

The free hydrochloric acid normally present in the stomach apparently affects ingested iron in two ways: it aids in the ionization of iron, and it prevents the formation of insoluble and undissociated iron compounds, particularly ferrous phosphate. The defective gastric secretion of the type observed in chlorosis must, therefore, play a role of some significance in the development of an iron-deficiency state. There is considerable evidence in favor of this view. Thus, Mettier and Minot[23] have shown that iron is more potent for blood formation when absorbed from an acid medium within the intestinal tract, rather than from an alkaline medium. Kellogg and Mettier[24] have observed that in some anemias due to chronic blood loss from peptic ulcer the alkalinization process associated with a Sippy regimen inhibits the absorption of iron contained in the food. The iron-balance studies of Fowler and Barer[25] indicate that achlorhydria interferes with the absorption of iron. Minot[26] has observed that cases of idiopathic hypochromic anemia with achlorhydria usually require distinctly larger doses of iron for the regeneration of hemoglobin at a maximal rate than cases of hypochromic anemia without achlorhydria do. He also noted that small doses of iron often have essentially no effect in the achlorhydric patient, but frequently can cause a definite hemoglobin increase when the gastric acidity is about normal. Achlorhydria therefore reflects an abnormal state in the gastrointestinal tract that interferes with the liberation and absorption of the dietary iron and leads to a depletion of the iron stores in the body. As the demands on the hemoglobin and iron stores become increased, anemia appears. In chlorosis these new demands are due chiefly to growth and menstruation (Heath and Patek,[1, 27] Heath[28]). According to this hypothesis, chlorosis is a deficiency disease conditioned in many cases by a disorder of the gastrointestinal tract.

TABLE 3. *Differential Features between Chlorosis and Primary Hypochromic Anemia.*

FEATURE	CHLOROSIS	PRIMARY HYPOCHROMIC ANEMIA
Age	14 to 20 years	Usually 30 to 40 years
Symptoms	Those of anemia and of gastrointestinal and menstrual disturbances	In addition to those of anemia, sore tongue, dysphagia (Plummer–Vinson syndrome), paresthesias and diarrhea
Skin	Texture normal; may present chlorotic or greenish tint; amount of pigmentation may be very scanty.	Often dry and inelastic; may present abnormal pigmentation; frequently, fissures at the angles of the mouth.
Hair	Normal	Frequently dry and prematurely gray
Fingernails	Usually normal	Frequently brittle, flattened, grooved and spooned
Tongue	Usually normal	Frequently atrophic
Splenomegaly	Rare[29]; slight splenomegaly in 10 per cent of cases[42]	Frequent (in 50 per cent of cases[32])
Blood	Leukocytes normal, occasionally increased; platelets normal, occasionally greatly increased.	Leukocytes normal or reduced; platelets usually reduced, occasionally normal[32, 44]
Bone marrow	Normal[9, 45] or hyperplastic[46]	Normoblastic hyperplasia[47–49]
Spontaneous venous thrombosis	In 2 to 3 per cent of cases[50]	None
Course	Remissions without treatment, with permanent cure common	Spontaneous remissions rare

Since the growth factor is equally operative in both sexes, one would expect to find occasional cases of chlorosis among males. Allbutt[29] and, more recently, Witts[30] have described the disease in the male sex. The latter investigator reported 5 cases; the diagnosis in 2 cases, however, is doubtful. Case 8 of the series reported here represents a striking case of male chlorosis.

Differential Diagnosis

There has been considerable diversity of opinion regarding the possible relation between classic adolescent chlorosis, summarized recently by Heath,[28, 31] and primary hypochromic anemia (also called "idiopathic hypochromic anemia," "simple achlorhydric anemia," "cryptogenic achylic chlor-anemia," "chronic chlorosis" and "hypochromic gastrogenous anemia"), first clearly defined by Faber[32] and described more recently in detail by Heath and Patek,[27] Witts,[33] Dameshek,[34] Minot[35] and Wintrobe and Beebe.[36] Thus, Naegeli[9] and Witts[10] are of the opinion that, in the absence of

achlorhydria and dysphagia, the microcytic hypochromic anemia of middle-aged women is allied to adolescent chlorosis. Heilmeyer[37] believes that of the two primary iron-deficiency states, chlorosis and primary hypochromic anemia, the former is associated with atony of the stomach and ptosis leading to defective iron absorption, and the latter with a chronic change in the gastrointestinal tract. Adamson and Smith[38] and Bloomfield[39] maintain that chlorosis and primary hypochromic anemia are the same disease. Of course, it is possible that the clinical picture of chlorosis has been altered and that the relatively recently recognized syndrome called "primary hypochromic anemia" is really not a new type of anemia, but rather an example of modified chlorosis. In fact, some authors do speak of present-day or latter-day chlorosis (Mills,[40] Schulten[41]). It seems to me, however, more reasonable to consider chlorosis as a definite disease entity, a view entertained by many observers, Heath and Patek[1, 27, 28, 31] and Minot[35] among others. It occurs in two forms, a severe one, which is rather infrequent, and a mild one, which is, according to Heath and Patek[27, 28, 31] and Davidson, Fullerton and Campbell,[42] quite common. It presents a number of characteristic features differentiating it from primary hypochromic anemia, as shown in Table 3. It must be admitted that atypical cases of both conditions are occasionally encountered that seem indistinguishable.

Summary and Conclusions

Classic adolescent chlorosis has not disappeared; and since histamine anacidity or hypoacidity is a common finding, it is probably a deficiency disease conditioned by a disorder of the gastrointestinal tract. In chlorosis, the red cells are hypochromic, small and flattened. The thrombocytes quantitatively are normal or increased. In other types of anemia, such as pernicious anemia, primary hypochromic anemia and anemia due to acute and chronic blood loss, the number of platelets is reduced and rises with improvement of the anemia. In chlorosis, on the other hand, there is an inverse relation between the platelet level (when elevated above normal) and the hemoglobin value. When the thrombocytosis is marked, it is a very significant, if not an essential, factor in the production of spontaneous venous thrombosis at times observed in these patients. Iron therapy cures the disease.

The term "chlorosis" should be discarded. The disease is more appropriately called "hypochromic iron-deficiency anemia of adolescence, frequently associated with achlorhydria."

371 Commonwealth Avenue

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IMPERFORATE HYMEN WITH HEMATOCOLPOS*

STANLEY O. HOERR, M.D.†

BOSTON

IMPERFORATE hymen with hematocolpos, an infrequently encountered condition, may present difficulty in diagnosis and is not without danger in treatment.[1-6] In 1939, Tompkins[1] collected 113 cases from the literature and noted that there had been deaths in 6 cases and severe pelvic infections in 9; he added 5 cases, with a single fatality and an additional case of pelvic infection. It is the purpose of this paper to add to the literature 7 cases seen and treated at the Peter Bent Brigham Hospital from 1914 through 1940; certain diagnostic and therapeutic features are re-emphasized.

CASE REPORTS

CASE 1. R. S., an 18-year-old girl, was admitted on December 4, 1914, complaining of back pain of 6 months' duration. Although the patient had been married for 5 months, coitus had never been successful. She had never menstruated. For 2 months, the pain had become severer, and was noted in the lower abdomen. She had had several bouts of urinary retention lasting 1 or 2 days.

Examination showed a young woman with well-developed secondary sexual characteristics. There was a slightly rounded, tender, fluctuant, lower abdominal mass rising just above the umbilicus. The hymen was imperforate and bulging, and carried an impulse from the abdominal mass. By rectum, a vaginal mass was palpable.

At operation, the hymen was incised under ether anesthesia, and approximately 750 cc. of reddish-brown, viscid fluid evacuated. This was not cultured. A small uterus and normal vaults were palpated. The patient was afebrile after operation, and was discharged on the 7th postoperative day.

Three years later, in 1917, the patient was seen in the Outdoor Department. She reported normal periods, and had borne a child 1½ years previously.

Comment. A normal pregnancy took place in a patient whose treatment was long delayed.

CASE 2. H. H., a 14-year-old girl, was admitted on August 21, 1931, complaining of intermittent lower abdominal pain of 2 years' duration. The attacks came at approximately monthly intervals and lasted 5 to 7 days; the pain included the lower back. She had never menstruated, nor had she had any urinary symptoms.

Examination showed a slightly obese young girl with normal secondary sexual development. There was an indefinite, slightly tender, mid-line, lower abdominal mass. The hymen was imperforate. By rectum a large fluctuant mass was palpable.

At operation, the hymen was excised under ether anesthesia, and a large amount of thick, "mucinous" old blood released. Culture was negative. The patient was afebrile after operation and was discharged on the 15th postoperative day.

Six months later, an examination in the Outdoor Department showed her to have a small normal uterus and cervix. In January, 1941, 9 years later, she reported normal and regular menstruation; although married for 1½ years, she had not become pregnant.

Comment. A return of normal function followed drainage.

CASE 3. R. J., a 13-year-old girl, was admitted on November 10, 1937. For about 4 months, she had noted increasing abdominal distention, and for 2 months she had had some lower abdominal pain, chiefly in the right lower quadrant. During this period, she had also experienced some difficulty in starting urination. She had never menstruated.

Examination showed a well-developed young girl with normal secondary sexual characteristics. There was a fluctuant, lower abdominal, mid-line tumor resembling an overdistended bladder, but persisting after catheterization. The hymen was imperforate and bulged slightly when pressure was exerted on the abdominal mass. By rectum, a transmitted fluid wave from the abdominal mass could be palpated, but there was not a marked bulging of the vagina.

At operation, the hymen was incised under ether anesthesia, and 900 cc. of chocolate-colored viscid fluid evacuated. The vagina was irrigated with saline. Culture of the fluid was negative. The patient was placed on constant urethral drainage for 6 days, remained afebrile, and was discharged on the 9th postoperative day. A questionable nubbin of cervix was the only portion of the internal genitalia that could be palpated.

Following operation, the patient never established a normal menstrual cycle, although her sexual development was in other respects normal. Her periods were scant and irregular, with intervals of amenorrhea lasting as long as 4 months. The flow was usually "watery" blood lasting only a few hours, although recently (December, 1940) she

*From the Surgical Service, Peter Bent Brigham Hospital.

†Instructor in surgery, Harvard Medical School; resident surgeon, Peter Bent Brigham Hospital.

had a 3-day flow with clots. A course of injections with one of the anterior pituitarylike hormones had no appreciable effect. The patient also suffered from vague abdominal pain, chiefly in the flank; this could never be explained, even after several readmissions for study, and a complete urologic investigation.

Comment. This patient may still develop a normal menstrual cycle; if not, one must suppose that the uterus was so damaged that it is incapable of normal menses. There is no evidence that the ovaries do not function.

CASE 4. N. G., an 11-year-old girl, was admitted on July 7, 1938. This patient, one of twins, had had a foul-smelling vaginal discharge for several weeks. Her twin sister had had 3 normal menstrual periods, whereas she had had none. There had been no abdominal pain or urinary symptoms.

Examination showed a well-developed young girl with normally developed secondary sexual characteristics. The abdomen was normal. The hymen was imperforate except for a pin-point opening just beneath the urethral orifice, from which pus could be expressed by pressure through the rectum. Fullness in the vagina was palpable by rectum.

Under ether anesthesia, a thick hymen was incised and a pint of thick, foul-smelling pus evacuated. The vagina was irrigated with saline. Culture of the pus yielded a mixed growth of *Staphylococcus aureus, Streptococcus hemolyticus* and *Escherichia coli.* A normal-sized uterus and normal vaults could be palpated. The patient was discharged, afebrile, on the 1st postoperative day, to receive vaginal irrigations and protargol suppositories at home.

Follow-up in January, 1941, 2½ years later, revealed that the patient was having regular, painless periods lasting 4 days.

Comment. The problem presented by this patient differed from that in the usual case, inasmuch as infection from below had taken place. Local immunity was already well established, and the treatment became that of any well-localized abscess. There was no need for a long hospital stay, and vaginal irrigations had a definite usefulness.

CASE 5. M. R., a 14-year-old girl, was admitted on August 30, 1939. For 3 days, she had had pain in the rectum, and for 2 days she had had progressively severe lower abdominal pain. She had never menstruated.

Examination showed a well-developed young girl. There was a tender suprapubic mass rising halfway to the umbilicus. The hymen was imperforate, thin and bulging. A tender, boggy mass was palpable anteriorly by rectum.

Without anesthesia, but with careful preparation of the vulva, the hymen was incised in the Outdoor Department, and 450 cc. of dark blood released. This was not cultured. The patient was admitted to the hospital for observation, and was discharged 36 hours later.

Four weeks later, a normal-sized uterus could be palpated by rectum. In February, 1941, about 18 months after operation, the patient reported periods occurring regularly every 28 to 30 days, lasting 4 to 7 days, and occasionally accompanied by lower abdominal pain.

Comment. The intern who cared for this patient evidently had no understanding of the potential dangers to which he was subjecting her. It was fortunate that there was no postoperative infection. A normal menstrual cycle resulted after drainage.

CASE 6. M. N., a 15-year-old girl, was admitted on February 22, 1940, complaining of increasingly severe lower abdominal pain of 4 days' duration. She had never menstruated or had any urinary symptoms.

Examination showed a thin, young girl with normal secondary sexual development. There was a soft, rather tender, lower abdominal mass rising halfway to the umbilicus. The hymen was imperforate and bulging. By rectum, a tender mass was felt anteriorly.

At operation under ether anesthesia, the hymen was excised and 1000 cc. of chocolate-brown old blood evacuated. Culture of this was negative. A small normal uterus and normal vaults were palpated. The patient remained afebrile after operation and was discharged on the 11th postoperative day.

In September, 1940, 6 months after operation, she reported regular, normal, painless periods lasting 6 days. Examination showed that the hymenal opening had contracted to a size of 5 mm.

Comment. A return of normal function followed drainage. The introitus requires further surgical opening, in spite of the supposed excision of the hymen at the time of operation.

CASE 7. M. L., a 15-year-old girl, was admitted on August 9, 1940, complaining of constipation, back pain and aching down the anterior thighs for the preceding 7 months. She had never menstruated or had any urinary symptoms.

Examination showed a thin, young girl with normal secondary sexual development. The abdomen was normal. The hymen was imperforate and bulging. An anterior mass was palpable by rectum.

Under gas-oxygen anesthesia the hymen was incised and 500 cc. of chocolate-colored thick fluid with some clots evacuated. *Bacillus subtilis* was cultured from this, but was regarded as a contaminant. No uterus or masses could be palpated. After operation, the patient remained afebrile and was discharged on the 10th postoperative day.

Five months after operation (January, 1941), she was seen in the Outdoor Department. A small uterus could be palpated by rectum. The hymenal opening was small. The patient reported regular, normal, painless periods every 28 to 30 days.

Comment. A return of normal function followed drainage.

SYMPTOMS, SIGNS AND DIAGNOSIS

Imperforate hymen with hematocolpos occurs in girls between the ages of eleven and eighteen years. The symptoms are a direct result of the accumulation of menstrual blood behind the imperforate hymen. An invariable feature of the history is the fact that the patient has never menstruated; yet, curiously, although understandably, this all-important information is rarely volunteered and is never a prominent symptom. The usual presenting complaint is lower abdominal pain, which is commonly associated with pain in the lower back and occasionally in the rectum or anterior thighs. The pain is often crampy and may be severe. It may occur at intervals corresponding to the time of the presumed menstrual periods (Case 2). As shown in Table 1, abdominal pain was a presenting symptom in 5 of

the cases reported in this paper, although in one (Case 1) pain in the back and in another (Case 5) pain in the rectum seemed equally important. It is noteworthy that although all 5 of these patients had an easily palpable abdominal mass, not one had apparently attached any significance to it, even if she had noticed it.

Difficult urination or even complete urinary retention frequently occurs in these cases.[1] Only

TABLE 1. *Summary of 7 Cases of Imperforate Hymen with Hematocolpos.*

Case No.	Age	Duration of Symptoms	Complaints			Abdominal Mass	Result†
			Abdominal pain	Backache	Difficult urination		
	yr.						
1	18	6 months	Yes	Yes	Yes	Yes	Normal menses, pregnancy
2	14	2 years	Yes	Yes	No	Yes	Normal menses
3	13	4 months	Yes	No	Yes	Yes	Scant and irregular menses
4	11	3–4 weeks	No*	No	No	No	Normal menses
5	14	3 days	Yes	No	No	Yes	Normal menses
6	15	4 days	Yes	No	No	Yes	Normal menses
7	15	7 months	No	Yes	No	No	Normal menses

*The only complaint was a foul vaginal discharge.
†All cases treated by incision or excision of the hymen.

2 of the reported patients (Cases 1 and 3) had urinary symptoms, and in neither were they prominent.

A careful physical examination cannot fail to establish the diagnosis. If a vaginal and rectal examination is invariably performed on girls or young women complaining of abdominal pain or difficult urination, cases of imperforate hymen with hematocolpos will not be overlooked, and cases in which the diagnosis is made only after laparotomy for real or supposed appendicitis,[2, 3] or after cystoscopy,[4] will be prevented. It is unfortunate that in this age group the physician most easily persuades himself that such an examination is undesirable and probably unnecessary. In most cases, there will be a visible bulge at the introitus. An error may be made in regarding a small normal hymenal orifice as imperforate if it is concealed by overlying folds of mucosa, but a probe will demonstrate an opening if present. By rectum, the blood-filled vagina will be felt anteriorly as a boggy mass. There will usually be a slightly tender, rounded, lower abdominal mid-line mass, contiguous with the vaginal mass.

Treatment

The treatment consists in surgical drainage through the vagina of the dammed-up menstrual secretions. These patients, however, are particularly susceptible to ascending infection, introduced from without, which may produce a fatal pelvic cellulitis or peritonitis. Such an infection may have its onset days or even weeks after surgical drainage, as shown by reported cases. Because of this special danger from sepsis, these patients should be hospitalized both for the operative procedure and for a postoperative period of ten to fourteen days. The operation must be carried out with scrupulous asepsis. Simple but generous incision of the bulging hymen may be sufficient, but if the hymen is thick and tough, excision may be preferable. A careful irrigation of the vagina in the operating room is probably without danger, but irrigations and douches must not be used in the postoperative period. After the fluid has been evacuated and while the patient is still under anesthesia, a rectal, rather than vaginal, examination should be performed to determine the presence of palpable adnexal masses. If such masses are found, an immediate exploratory laparotomy should be considered, as suggested by Tompkins,[1] to remove or drain the blood-distended tubes.

In the postoperative period, the points to be stressed are bed rest in Fowler's position and the maintenance of strict perineal cleanliness. Some surgeons advocate a constipating regime for four or five days, although this does not appear to be necessary. A short course of sulfanilamide as a prophylactic is worthy of consideration. No restrictions on patients are required, once the period of hospitalization is over. Nevertheless, it is sound practice to advise against douching, tub bathing or vaginal examinations until two menstrual periods have passed, as urged by Tompkins.[1]

Prognosis

The possibility of a fatal ascending infection has been pointed out; this should be avoidable with the exercise of sufficient care. Most of these patients start a normal menstrual cycle, and some go on to child-bearing. The oldest patient (Case 1) in this group, aged eighteen, in whom one would naturally expect the severest damage to the uterus and tubes, bore a child eighteen months after operation. On the other hand, another patient (Case 3), aged thirteen at operation, subsequently had irregular and very scanty periods. One should neither be too pessimistic

with the late case, nor promise too much with the early one.

Summary

Imperforate hymen with hematocolpos is a syndrome occurring in girls between the ages of eleven and eighteen who have never menstruated. The usual presenting symptom is abdominal pain, often associated with back pain. There may be a history of difficulty in urination. The diagnosis is established by demonstrating the imperforate hymen, which is often bulging, and by palpating the blood-filled vagina through the rectum. There is usually an associated suprapubic mass.

Treatment consists of vaginal drainage of the dammed-up blood by incision or excision of the hymen under the most scrupulous asepsis; if adnexal masses persist after drainage, an immediate laparotomy for further surgical treatment of the tubes must be considered. The postoperative regimen consists of rest in bed in Fowler's position for ten to fourteen days, strict perineal cleanliness and postponement of douches, tub baths and vaginal examination until several menstrual periods have passed. The prognosis for a normal menstrual cycle is good; normal pregnancies are known to occur.

Seven cases seen and treated in the Surgical Service of the Peter Bent Brigham Hospital from 1914 through 1940 are reported. There were no postoperative infections in this group, and no deaths. One patient is known to have had a subsequent normal pregnancy.

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THE SIGNIFICANCE OF A HISTORY OF ASTHMA WITH REFERENCE TO SEROTHERAPY*

David D. Rutstein, M.D.,† Edward S. Rogers, M.D.,‡ and Isabel McCaffrey, A.B.§

Albany, New York

A RECENT circular letter[1] prepared by the Committee on Chemotherapeutic and Other Agents and the Subcommittee on Infectious Diseases, of the Division of Medical Sciences, National Research Council, included a discussion of the contraindications to the use of serum in patients with a history of allergic manifestations. The circular letter stated, "Serum should never be given to patients who have a history of asthma of any type or to those who have a history of hay fever." Because the circular letter carries the weight of authority, the statements contained in it are likely to influence treatment of the civilian population, as well as that of members of the armed forces. Since the sentence quoted was at variance with the impression gained from a previous study of reports on the use of antipneumococcus horse serum in New York State, it was considered appropriate to subject these reports to careful analysis regarding the point at issue. This seemed particularly important because a thorough review of the literature concerning immediate serum reactions in man failed to reveal any study comparing the incidence of immediate serum reactions in patients with and without a history of asthma.

In the review of the literature, no case of a death associated with a reaction to antipneumococcus horse serum in an asthmatic patient was found. Bullowa[2] reported 8 fatal cases following the injection of antipneumococcus horse serum, none of which had a preceding history of asthma, and Heffron[3] reported 2 fatal cases, neither of which had a history of allergy preceding the injection of the serum. Heffron[4] also reported, "In the course of the Pneumonia Study and Continuing Program in Massachusetts, at least 15 patients with a history of asthma and 2 with a history of hay fever were treated without unfavorable reactions."

Between January 1, 1937, and March 31, 1939, 3215 reports on the use of antipneumococcus horse serum in which information of the history of allergy was recorded were received by the New York State Department of Health. Of these, 101 (3.1 per cent) indicated a history of asthma, although

*From the Bureau of Pneumonia Control, New York State Department of Health.

†Director, Cardiac Bureau, New York State Department of Health; assistant professor of medicine, Albany Medical College.

‡Assistant Commissioner for Medical Administration, New York State Department of Health; assistant professor of medicine, Albany Medical College.

§Assistant statistician, New York State Department of Health.

in no case was the asthma related to a history of specific sensitivity to horse emanations. This study must not be interpreted to include patients with a history of specific sensitivity to the animal from which the serum was derived.

As shown in Table 1, the incidence of immediate

TABLE 1. *Incidence of Reactions Among Pneumonia Patients Treated with Specific Antipneumococcus Horse Serum, according to History of Asthma.*

GROUP	HISTORY OF ASTHMA		NO HISTORY OF ASTHMA	
	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Thermal reaction	24	24.7*	515	16.5
Circulatory reaction	10	9.1*	117	3.8
Anaphylactic reaction	17	22.6*	227	7.3
Miscellaneous reactions	13	17.3*	278	8.9
Cases with reaction	46	45.5	922	29.6
Cases without reaction	51	50.5	2102	67.5
Cases unknown as to reaction	4	4.0	90	2.9
Totals	101		3114	

*Adjusted to allow for older age distribution in cases with history of asthma.

serum reactions in the patients with asthmatic histories was greater (45.5 per cent) than that in those without such histories (29.6 per cent). This difference was found to be most significant in those patients having the anaphylactic† type of reaction. However, the incidence of fatal reactions

TABLE 2. *Incidence of Fatal Reactions Among Pneumonia Patients Treated with Specific Antipneumococcus Horse Serum, according to History of Asthma.*

GROUP	NO. OF CASES	FATAL REACTIONS
Cases with history of asthma	101	1‡ (1.0%)
Cases with no history of asthma	3114	22 (0.7%)
Total	3215	23 (0.7%)

‡This patient was sixty-five years of age, with a long-standing history of cardiovascular disease and a three-year history of asthma. The conjunctival and intradermal tests were negative, and he received 1 cc. of serum intravenously without reaction prior to the fatal dose. The reaction was circulatory in nature.

was approximately the same in both groups of patients (Table 2). These data suggest caution in the administration of serum to asthmatic patients, but do not appear to justify the prohibition of its use in those patients with asthma not related to specific animal-protein sensitivity.§

Further evaluation of the importance of asthma can be derived from a study of the fatality rates of serum-treated pneumonia patients according to asthmatic status. The fatality rates of patients with and without asthmatic histories did not significantly differ from each other after correction for differences in age and bacteremia (Table 3).

TABLE 3. *Case Fatality Rates Among Pneumonia Patients Treated with Specific Antipneumococcus Horse Serum, according to Incidence of Reactions and History of Asthma.*

GROUP	HISTORY OF ASTHMA			NO HISTORY OF ASTHMA		
	NO. OF CASES	NO. OF DEATHS		NO. OF CASES	NO. OF DEATHS	
Cases with reaction	46	12	(17.5%‖)	922	128	(13.9%)
Cases with no reaction	51	15	(14.4%‖)	2102	318	(15.1%)
Cases unknown as to reaction	4	0		90	16	(17.8%)
Totals	101	27	(16.8%‖)	3114	462	(14.8%)

‖Adjusted to allow for older age distribution and larger proportion of positive blood cultures in cases with history of asthma.

Moreover, the mortality rates from pneumonia among patients with or without a history of asthma were not significantly different whether or not immediate serum reactions occurred.

In view of these findings, and in the absence of contradictory data in the medical literature, it is fair to conclude that a history of asthma due to other than specific sensitivity to the animal from which the serum is derived is not an absolute contraindication to serum therapy.

†In a study, recently published elsewhere,[5] of 25 patients with fatal serum reactions and 790 with nonfatal immediate serum reactions of all degrees of severity, it was shown that immediate reactions following the injection of antipneumococcus horse serum can be divided into four categories: thermal, anaphylactic, circulatory and miscellaneous, the clinical pictures of which are defined. In that study, all but one of the fatal serum reactions were shown to be circulatory in nature and not related to recognizable protein hypersensitivity.

§It is recognized that injection of horse serum may cause sensitization, which increases the dangers of its subsequent administration. However, no evidence can be found in the literature that persons with hay fever or asthma are more easily sensitized with horse serum or rabbit serum than normal persons. Since our series does not contain enough patients who had received serum previously, we are unable to settle this point.

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CLINICAL NOTE

A SEVERE CASE OF PARATHYROID ADENOMA*

CHARLES S. CURTIS, M.D.,† AND
EVARTS G. LOOMIS, M.D.‡

SAINT ANTHONY, NEWFOUNDLAND

THE following case of adenoma of the parathyroid gland is reported because of the large size of the tumor, the extensive bony changes with multiple fractures and the excellent bony recovery that followed operation.

CASE REPORT

S. N., a 29-year-old fisherman, was admitted on July 18, 1939, complaining of loss of the use of both legs and the right arm. The onset of illness was a dull boring pain in the right lower leg 2 years before admission. This persisted for a year, and then the patient noticed a swelling in the lower third of the right leg. This increased in size, and the leg gradually became bent, distortion increasing as he walked. He kept moving about for several months, but did not do any work. About the time of the appearance of swelling, the pain left him, and he had felt none since. Four months before admission, while going downstairs, the patient slipped and struck his right arm. He gave no history of distortion at that time, but there was loss of power in the arm. Although there was no pain in the arm, there was a feeling of deadness. After being in bed for some months, he noticed one morning that his right arm was angulated and that there was unnatural mobility of the bone.

There were no symptoms referable to the gastrointestinal tract or the cardiovascular and genitourinary systems. The past history revealed that the patient's back had been bent and that he had had shortening of the right leg, with some muscle atrophy, since early childhood, although he apparently had not noticed it himself until the onset of his illness. There was no familial history of any such symptom complex. The home conditions were fair, but the patient's nutrition was poor.

Physical examination showed a short, thin, hunch-backed man who was unable to stand up but in no pain. The skull was small and wedge-shaped, with no apparent increase of thickness. The spine was fixed, with a marked dorsal kyphosis and slight scoliosis. The thorax was compressed laterally, and the chest was thin and pigeon-shaped. The left clavicle was sharply angulated at the outer third, with swelling above that point. The right arm showed a sharp angulation and undue mobility in the mid-portion of the humerus. Both hips showed loss of abduction and external rotation. Flexion of the right knee was limited. There was marked bowing of the outer third of the right tibia. Examination of the eyes showed active pupillary reflexes. The gums were foul. There was no palpable enlargement in the region of the thyroid gland. No enlargement of lymph nodes was observed. The blood pressure was 120/70. The examination was otherwise negative.

Ophthalmoscopic examination showed an area of sclerosis in the lens.

Examination of the blood showed a red-cell count of 3,700,000 with a hemoglobin of 65 per cent (Sahli), and a white-cell count of 6400. The bleeding time was 3 minutes, the clotting time 3 minutes and 30 seconds. The urine was normal. As the means for determining the serum calcium were not on hand, a specimen was sent to Royal Victoria Hospital, Montreal; it was reported as 13.2 mg. per 100 cc.

X-ray examination on July 19 showed fractures of the right humerus, right ulna and both femoral necks (Fig. 1), a supracondylar fracture of the left femur and a fracture of the right tibia. The x-ray films also showed generally decreased calcification of all the bones, particularly evidenced by the thinning of the bony cortex and the irregular cystic appearance of some of the diaphyses, especially in the right humerus and the tibia, mostly in the regions of fracture. X-ray films of the skull were not remarkable. There was a calculus in the left kidney pelvis.

FIGURE 1. *Preoperative X-ray Film of Pelvis (taken July 19, 1939).*

Note the fractures of both femoral necks, the poor definition of the iliac crests, the thinning of the cortex of the femurs, and the scarcity of trabeculations in all bones.

On August 17, under avertin anesthesia, an operation was performed. On elevation of the left lobe of the thyroid gland, a sizable reddish-yellow encapsulated tumor was seen in intimate contact with the posterior capsule of the gland. The tumor was dissected free and removed by blunt dissection. Posteriorly, the tumor was found to be in contact with the trachea. Bleeding, which was moderate, was controlled and the wound closed. A blood transfusion was given postoperatively, and the patient made an uneventful recovery.

*From St. Anthony Hospital, International Grenfell Association.
†Medical superintendent, International Grenfell Association.
‡Chief surgeon, St. Anthony Hospital.

Pathological examination showed the specimen to be a friable, reddish-gray tumor, measuring 4.5 by 2.5 by 2.0 cm. and weighing 11.3 gm. Microscopic examination showed the structure to be a compact mass of small cuboidal cells, with large dark-staining nuclei and little cytoplasm. These cells showed a slight tendency to form small round glands, but for the most part there was no definite structural pattern. A diagnosis of hyperparathyroid adenoma was made, which was confirmed by Dr. Harrison Martland, of the Newark (New Jersey) City Hospital.

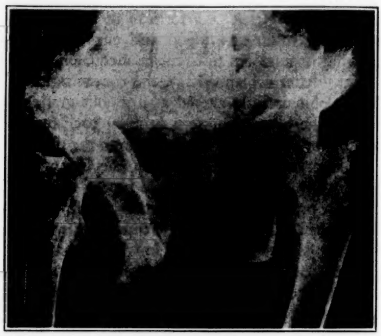

FIGURE 2. *Postoperative X-ray Film of Pelvis (taken October 22, 1940).*

Note the increased density of all bones, with distinct trabeculation, and the good definition of the bony pelvis.

During the following winter, attempts were made to improve the position of the fractures with Buck's extension and casts. On November 27, the blood calcium was reported by Royal Victoria Hospital to be 8.9 mg. per 100 cc., and the phosphorus to be 4.6 mg.

The patient was discharged on June 1, 1940, with a brace for the right leg. By this time there was good evidence of fibrous union.

The patient was readmitted for a check-up on October 17. At that time he was able to get about with crutches, had no complaints and claimed that he felt fine. There was good clinical union of the humeral, tibial and femoral fractures, and no limitation of movement of the right arm. There was good flexion and extension of the hips, but slight limitation of abduction of the left hip. The blood calcium on November 1 was 10 mg. per 100 cc. X-ray films taken on October 22 (Fig. 2) showed the cortex of both femurs to be much wider and denser. There was a marked increase in density of all bones, with new and definitely increased calcification of the femurs and iliums. The iliums, which previously appeared ill-defined in contour, had taken on their characteristic shape and structure.

SUMMARY

An unusual and interesting case of parathyroid adenoma is reported.

MEDICAL PROGRESS

WAR MEDICINE*

With Special Emphasis on the Use of Blood Substitutes

CHARLES A. JANEWAY, M.D.†

BOSTON

WITH the threat of war becoming so real, two publications should prove very useful for those who wish to keep abreast of developments in military medicine. The *Bulletin of War Medicine*, published in England, contains abstracts of practically all pertinent articles. *War Medicine*, published in this country, contains general reviews on important topics and abstracts of carefully selected articles, all of which are extremely well done.

During the past year, one outstanding feature of the war has been the heavy aerial attacks to which the cities of Great Britain have been subjected. This type of warfare, aimed at the civilian population, is new, and this report is concerned with some of the medical problems that it raises.

BLOOD AND BLOOD SUBSTITUTES

Observers returning from England, as well as reports in the British literature, stress the severity of the casualties occurring as a result of air raids. For this reason, an understanding of the pathogenesis of shock and its treatment is of tremendous value. Although there is great dispute about many details of the shock syndrome, enough has been learned in recent years to make it possible to treat most patients intelligently, particularly those with shock of traumatic origin.[1, 2]

All articles in this series will be published in book form; the current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

*From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School.

†Instructor in medicine and in bacteriology and immunology, Harvard Medical School; associate in medicine, Peter Bent Brigham Hospital.

Following a severe injury, so-called "primary shock" frequently occurs. This is really a condition of vascular collapse, in which the tone of the peripheral vessels is diminished reflexly, as a result of nervous or psychic stimuli. The vascular bed is dilated to such an extent that the volume of blood becomes insufficient to maintain an adequate venous return to the heart, and thus an adequate output to the periphery. It may be difficult to distinguish this form of collapse from true secondary shock; therefore, all patients admitted with a feeble pulse and lowered blood pressure should be treated immediately for collapse. This treatment involves administering morphine if there is pain, getting the patient warm with blankets and sometimes hot fluids (tea, of course, in England), and putting the patient in shock position with the feet elevated, because gravity plays such an important part in the pooling of blood. If the patient does not quickly improve under these conditions, true secondary shock is probably present.

Most workers agree that in secondary shock there is an insufficient volume of blood to maintain an adequate peripheral circulation, not because of vasodilation (vasoconstriction is usually present), but because of loss of blood or one of its components. This deprivation may come about in a number of ways. In extreme dehydration as in diabetic acidosis or severe diarrhea, it is caused by a loss of water and electrolytes. On the other hand, in hemorrhage it results from a loss of blood, and in burns or severe trauma it results from the oozing of plasma into the injured area. The immediate effects are concentration of those elements of the blood that are not lost, vasoconstriction, manifested by a cold and clammy skin and a thready pulse, and the subjective symptoms of sweating, thirst, anxiety and nausea. If the state of shock continues long enough, general capillary damage may occur, with leakage of plasma throughout the body, thus further exaggerating the symptoms.

In burns and crushing injuries with marked concentration of the red cells, the treatment of choice is the restoration of the lost plasma. Saline infusions are at best of temporary benefit, since the fluid is rapidly lost from the circulation, thus aggravating the condition by sweeping out the proteins of the blood, which are so necessary for the maintenance of its osmotic pressure.[3] On the other hand, in hemorrhage, the ideal therapy is the replacement of whole blood, since both red cells and plasma have been lost. In normal persons, there is a considerable margin of safety in circulating hemoglobin, and the patient with an acute hemorrhage develops symptoms from diminished blood volume far sooner than from loss of hemoglobin. Hence, any form of therapy that restores the volume of blood and enables the remaining hemoglobin to circulate adequately is sufficient. After a hemorrhage, the concentration of hemoglobin is little altered at first, but gradually falls as the blood volume is brought back to normal by the production of plasma from the patient's own reserves.[4] However, when the hemoglobin falls below a certain level, this process of hemodilution proceeds only to a certain point.[5] Therefore, when a relatively low hemoglobin value is found to begin with, it seems unwise to administer plasma alone. British experience has borne this out. Whereas plasma is extremely effective in the treatment of most air-raid casualties, its use in the treatment of a small series of patients with bleeding ulcers whose hemoglobins were 50 per cent or less before treatment was frequently accompanied by reactions and a fall in blood pressure.[6]

In addition to the use of various types of parenteral fluid, as discussed above, the treatment of shock involves the administration of oxygen whenever possible,[7, 8] since anoxia is an important cause of capillary damage. Warmth, the Trendelenburg position and morphine are also valuable adjuncts to therapy.

There are a number of ways in which whole blood can be made available in emergencies. In the German army, men are assigned to detachments according to their blood groups, so that if any person in a particular unit needs a transfusion he may receive one from another member of the group. This is scarcely applicable to civilian populations. A second method is the listing of all universal donors,* who comprise some 45 per cent of the population. These people can then serve as donors in emergencies. If care is taken to eliminate those universal donors who have high titers of isoagglutinins, this is a feasible step, since it is usually those with high titers who cause the trouble that inevitably occurs when universal donors are used indiscriminately.

Witebsky et al[9] have recently shown that it is possible to obtain in pure form the A and B factors that are responsible for the specificity of the red cells of Groups A and B. These are mixed in the proper proportion in sterile ampoules, and the contents of an ampoule, when added to 500 cc. of Group O blood, instantly combine with and neutralize the agglutinins. This blood can then be used indiscriminately without previous cross-

*Group O by the international nomenclature, Group IV by Moss, or Group I by Jansky.

matching. Witebsky emphasizes the fact that the blood must be taken from a true universal donor, and suggests that such donors be grouped not only by testing their cells against known serums, but also by testing their serums against known cells. These group factors are nonantigenic, and the subjects do not develop an increased titer of isoagglutinins as a result of the injection of blood neutralized with this material. Witebsky reports quite a large series of successful transfusions of this type. Further experience will be necessary before this type of transfusion can be recommended for any but emergency use. Wiener and his co-workers[10] report a reaction from a second transfusion of Group O blood in a patient of another group. The recipient developed anti-O agglutinins as a result of the first transfusion, which reacted with the donor's cells on the second transfusion. Thus, the repeated use of neutralized Group O blood might be dangerous.

It is probable that fresh blood will not be used so much for emergencies as stored blood, since the latter can be kept on hand in adequate amounts and is ready for use at any time. There has been an enormous amount of work on stored blood since the institution of blood banks in many hospitals in this country. The use of cadaver blood has been recommended by certain Russian investigators.[11] It does not require the addition of an anticoagulant, and large amounts of it may be obtained from a single donor. However, when very large amounts of blood are necessary, the difficulties of such collection are too great and its advantages too slight to make it practicable. Placental blood has likewise been used[12, 13] and should provide a valuable supply of blood for the preparation of plasma in general hospitals. It has a low isoagglutinin titer and a low lipoid content, giving a very clear plasma.[14] Ham[15] has recently discussed the relative advantages of fresh and stored blood. For the treatment of shock and hemorrhage, stored blood is as effective as fresh blood, and sufficient case reports are now available to show that the incidence of reactions is no greater.[16, 17]*

The changes that take place in stored blood have been the subject of exhaustive study by a number of investigators[18–25] whose results are in general agreement. Certain components of the blood deteriorate very rapidly. These are the leukocytes, particularly the granulocytes, which disintegrate within the first two or three days, and the platelets, which likewise disappear very rapidly. The prothrombin and complement titers fall off somewhat more slowly, whereas the red blood cells do not diminish appreciably in number for a much longer period. Since it is the plasma and red blood cells that are important in the treatment of shock, a great deal of attention has been paid to methods of preservation that will prevent the hemolysis of red blood cells. With the ordinary citrate anticoagulant in use in most hospitals, stored blood should not be used after more than ten days, because at the end of this time an appreciable proportion of the red cells have begun to hemolyze. Certain measures are effective in the prevention of hemolysis. The exclusion of air by filling the bottle as full as possible is helpful, particularly when blood is to be transported, since there is less agitation of the red cells under these circumstances. Dilution is also an effective means of diminishing hemolysis, but the addition of glucose is most important. This discovery is not new, but goes back to the work of Rous and Turner[26] in 1916. DeGowin and his co-workers[27] have given a great deal of attention to these problems and use a modification of the Rous–Turner anticoagulant mixture routinely. Five hundred cubic centimeters of blood is drawn into a bottle containing a mixture of 650 cc. of 5.4 per cent anhydrous dextrose and 100 cc. of 3.2 per cent dihydric sodium citrate in water chilled to -5°C. The blood is drawn into a bottle of such capacity that, when mixed with the anticoagulant, the container is almost completely filled. Blood taken in this way can be used up to thirty days after bleeding without any increase in the incidence of reactions. DeGowin and Hardin[28] have shipped blood by truck and by plane for many miles in iced containers and have used it after transportation in an attempt to show that this is a practicable procedure for military use. Furthermore, DeGowin and his associates[29] have shown that the incidence of reactions is not increased by administering blood as soon as it is removed from the refrigerator or iced container. DeGowin's recommendations deserve serious consideration, and, where hospital blood banks are in operation, the use of this particular anticoagulant mixture is to be commended, since it will at least double the useful life of stored blood. The drawback is that the blood is diluted, and therefore a larger volume has to be administered with each transfusion, which is a disadvantage when congestive failure or hypertension is present. Also, the increased bulk uses up valuable space in transportation.†

*Jewesbury[16] summarizes the published literature on the incidence of Grade III reactions (frank chills) as follows: fresh blood (700 transfusions), 6.0 per cent; stored blood (4973 transfusions), 4.7 per cent.

†Various modifications have been proposed to reduce the dilution factor. Denstedt and his co-workers[30] recommend the following: blood, 5 parts; 3.2 per cent sodium citrate, 1 part; and 5.4 per cent dextrose, 1.5 parts. Jewesbury[16] used 360 cc. blood and 180 cc. of an anticoagulant mixture containing 1.05 per cent sodium citrate and 3 per cent dextrose in 0.85 per cent saline solution. Barton[31] takes blood into 2.5 per cent sodium citrate solution, and adds 50 cc. of 25 per cent aqueous dextrose solution for every 500 cc. of blood after the blood is drawn.

Considerable attention has been directed to the rise in potassium content of the plasma during the storing of blood.[32–34] This is not the result of hemolysis, since the potassium level rises to a peak of between 60 and 100 mg. per 100 cc. in the first five days of storage, and does not increase so fast thereafter. It probably diffuses from the red cells in addition to being liberated by the disintegrated white cells. Blood with this potassium content has been shown to be innocuous by DeGowin et al.,[35] although some workers have suggested that certain unexplained reactions have arisen from its use. The sodium content of the red cells becomes about four times normal during storage, and this produces an increase in the sodium content of the red blood cells of the recipient after transfusion. However, within twenty-four hours, the sodium content of the recipient's red blood cells returns to normal, indicating the restoration of cell electrolyte balance, once these abnormal cells are put into circulation.[36]

Several groups of workers[36–38] have studied the fate of the red cells of stored blood after transfusion. This is done by various modifications of the technic devised by Ashby. Such studies indicate that the cells of stored blood survive nearly as well as the cells of fresh blood, provided the cells do not show an increase in fragility or the blood an appreciable amount of hemolysis before it is used. Certain cells of stored blood become more fragile on storage, and, once transfused, these cells are hemolyzed in the body of the recipient. Thus with ordinary citrated blood kept longer than seven days, — in which tests show that an increased in vitro fragility is present, — bilirubinemia and jaundice may develop in the recipient during the first twenty-four hours.[37–39] Even under these circumstances, it is pointed out that an appreciable number of the red cells survive and that iron from the hemolyzed cells may be utilized to produce new hemoglobin. Wiener and Schaefer[39] have shown that every day of storage in citrate diminishes by about six days the life of a red cell after transfusion, and that it is therefore bad practice to use blood kept more than ten days with plain sodium citrate solution, or more than thirty days with dextrose-citrate solution. They also claim that dextrose, when added to the anticoagulant, increases the life of the cell after transfusion as well as before.

A final point of significance in the use of stored blood is the necessity for having a filter of some type in the outflow line. Small clots are prone to form in both citrated plasma and blood on storage in the cold, and it is essential to use some method of removing such clots if reactions are to be avoided. Various types of filters, of wire or gauze mesh, have been devised and are available in most commercial outfits.

Although blood is ideal for the treatment of hemorrhage as suggested above, plasma may be used to restore the blood volume and maintain an effective circulation. In crushing injuries, burns, peritonitis and pulmonary edema from poison gases, shock occurs mainly from the loss of plasma, and plasma is not only satisfactory but far better than blood as a therapeutic agent. Since plasma can be kept much longer than blood and, when pooled, can be used without previous cross-matching, it has come into wide use in emergency therapy. Many papers[40–45] in the literature stress the value of plasma in the treatment of secondary shock, both experimental and clinical. It has been used on a wide scale in England in the treatment of shock and acute hemorrhage, where it has become customary to give 500 to 1000 cc. to a shocked patient, and if further therapy is necessary 500 cc. of blood before administering more plasma.[46*] The studies of a number of workers, particularly Scudder and his associates,[48] have emphasized the benefit of simple observations such as the hematocrit, hemoglobin and plasma specific gravity values in following shock patients, because they give valuable information *before changes in blood pressure occur.* In air-raid casualty stations, little more is possible than an estimation of the hemoglobin content of the blood and a close watch of the patient's blood pressure. All the English workers have pointed out that blood pressure is a far more reliable guide than pulse rate, and that the effect of the administration of plasma on the hemoglobin content of the blood is a very good index of whether blood as well as plasma is necessary.[46†] If the hemoglobin is lowered well below normal by the administration of a liter of plasma, the patient should receive some whole blood. As pointed out above, when the hemoglobin is already quite low as a result of spontaneous hemodilution, prolonged oozing of blood or previous anemia, the administration of plasma may be harmful.

Pooled plasma can be used in extremely large

*Some idea of the volumes of blood and blood substitutes necessary for the treatment of severely shocked patients may be obtained from a report of the treatment of an injured flyer of the Royal Air Force, who received 2160 cc. of pooled plasma and 2700 cc. of Group O blood in sixteen hours, with eventual recovery.[47]

†Bushby, Kekwick and Whitby[46] point out that the blood volume, and hence the approximate amount of blood lost (by subtracting the blood volume from the normal estimate of 40 cc. per pound), can be calculated after plasma transfusion by the following formula:

$$\frac{\text{Blood volume (cc.) before plasma}}{\text{Blood volume (cc.) + plasma (cc.) given}} = \frac{\text{Hematocrit or hemoglobin per cent after plasma}}{\text{Hematocrit or hemoglobin per cent before plasma}}$$

doses without cross-matching. Levinson and Cronheim[50] have shown that the isoagglutinins in a particular sample of serum are markedly decreased if it is mixed with several other samples of human serum. These observations have been extended and amplified by British workers,[51] and it is apparent that this suppression of the isoagglutinins results from their neutralization by blood-group substances A and B present in the plasma. The proportion in which plasmas should be pooled depends on their relative agglutinin contents, but a formula that has been used with success in England depends on mixing two parts of Group O plasma with four parts of Group A plasma and one part of Group B plasma. Many workers merely pool eight to ten plasma samples without regard to blood groups.[52] It is possible that a plasma with a very high agglutinin content pooled in this routine fashion might still cause trouble, and if hemolytic reactions occur with pooled plasma, the isoagglutinin content of the pool should be determined.

The use of plasma in the treatment of shock is a vital subject and one in which a great many disputes are going on among workers in the field. The first dispute concerns the method of preservation and preparation of the plasma. If plasma is not separated in the first two days after the blood is drawn, its potassium content will be relatively high. However, there is little evidence that this is particularly harmful. In most blood banks, it is now the custom to separate the plasma after the expiration date of the stored blood, although it doubtless would be ideal to separate the plasma in the first twenty-four hours. A number of methods have been devised for preservation. If plasma is to be preserved in its liquid state, there are two dangers: first, the formation of small clots, which can be taken care of by using a filter in the apparatus for injection, and secondly, bacterial contamination.[53, 54] Experiments by British workers[55] have shown that no antiseptic or bacteriostatic agent is very satisfactory in plasma. Proflavine in a dilution of 1:100,000 is probably the best, but is not effective for more than two or three days. The sulfonamide drugs, although quite effective as bacteriostatic agents in whole blood stored in the cold, are not effective in plasma stored either in the cold or at room temperature. Therefore, very strict asepsis must be maintained in all the processes of collection, pooling and bottling of plasma. If possible, everything should be done with a closed system, and the English have come to the conclusion that if plasma is to be kept in the liquid state for any length of time it must be passed through a bacteriologic filter to ensure sterility. It is very difficult to filter plasma through a Seitz filter, which is the most convenient type to use, because calcium present in the asbestos filter pads combines with the citrate and clotting occurs. Bushby and his co-workers[56] have devised a method for washing the pad intermittently with a strong citrate solution, so that the plasma may be filtered in reasonable amounts. Thalhimer[57] removes most of the calcium from the pads by soaking them in hydrochloric acid. Another group of workers[54] in England add a solution of calcium chloride to the plasma in a flask containing glass beads. The plasma is then agitated. As clotting occurs, the clot is broken up into small masses by the agitation, and a large yield of serum is obtained. This defibrinated fluid can be filtered readily through a Seitz filter and, although it contains a considerable amount of calcium, has apparently been used without reactions.

Probably the most effective way to preserve plasma is to freeze it.[58] In hospitals, where refrigeration is no problem, this is the ideal method. The plasma may be separated by centrifugation in closed bottles, aspirated aseptically into a pooling bottle, reaspirated into 250-cc. or 500-cc. bottles as pooled plasma, and frozen within a few hours of being drawn. It may be frozen and stored in an ordinary low-temperature mechanical refrigerator used commercially for frosted foods, which maintains a temperature of −10 to −15°C. It can be kept in this manner for very long periods without danger of bacterial contamination, or deterioration of such unstable fractions as prothrombin and complement. When ready for use, it may be rapidly thawed at 37°C. and administered to the patient.

When refrigeration is impossible, dried plasma can be used. Three general methods of drying have been advocated.[59–71] The first, originally designed by Thalhimer[59] for the concentration of convalescent serum, consists in rotating the plasma in cellophane bags in a stream of warm dry air. The water evaporates, until finally the plasma solids are left as a dry powder in the bag. This method, which has been advocated by Hartman[60] and used successfully by him, is valuable because of its cheapness and simplicity. The second method, which makes use of vacuum distillation as the plasma is sprayed into a heated chamber, seems less effective because it requires heating and the transfer of the product from one container to another, with a consequent danger of contamination.[61, 62] The third method of drying de-

pends on evacuation and consequent evaporation of water from the frozen plasma. One process involves the preliminary rapid freezing of the material, which then remains frozen throughout the evacuation process by virtue of the rapid evaporation of water vapor.[63–67] The other type involves freezing as a result of the evaporation itself, which occurs very rapidly as the pressure in the container falls to nearly a complete vacuum.[68–71] There are variations of these methods, involving the type of apparatus used to trap the water coming off the plasma, but the principles involved are much the same. Such plasma desiccated from the frozen state is very little altered, since it is frozen very rapidly and has an extremely low moisture content. In this state, the plasma will keep for years if it is protected from the penetration of water vapor from the atmosphere. To ensure this, the material must be kept in sealed glass ampoules or else in rubber-stoppered bottles inside evacuated or nitrogen-filled containers. It can be reconstituted by the addition of appropriate amounts of sterile distilled water as normal plasma or concentrated plasma of varying strength. Such dried plasma will obviously be extremely useful as a readily available blood substitute for use in out-of-the-way places.

Besides disputes about the method of preparation and preservation of plasma, there is an argument about whether serum or plasma may be used interchangeably, and another about whether concentrated, dilute or isotonic plasma should be used in the treatment of shock. Adequate evidence is not available on either of these points to date. However, incomplete reports indicate that, for some reason as yet not understood, reactions are more frequent with serum than with plasma, whereas reactions are no more frequent with plasma than with blood.[72–74] Those who have had experience with the preparation of serum do not seem to have had many reactions with their own product,[54, 75–78] but serum cannot be recommended for general use until more evidence regarding its innocuousness is at hand. Its main virtue is that it does not clot on passage through a Seitz filter, and hence it is more easily prepared on a large scale.

The dispute concerning the value of concentrated plasma or serum cannot be settled. Hill and his co-workers[79–81] have used four-times concentrated plasma a great deal in the treatment of shock in hospital patients, and their clinical results seem very favorable. In certain English reports, concentrated serum produced reactions, and often thrombosis of the vein, but this product was concentrated by partial evaporation of the water from the serum, and had not been reconstituted from the dried state. It seems reasonable to expect that concentrated plasma is effective in the treatment of shock when adequate reserves of fluid are present in the tissues. On the other hand, in the presence of dehydration, the administration of a hypertonic solution is obviously contraindicated. More work will need to be done on this phase of the question.

An entirely new approach to therapy with blood plasma has been proposed by Cohn and his associates.[82] Instead of using whole plasma for every condition, he proposes to use fractions of the plasma for specific purposes. In shock, the important point is to restore blood volume. The most useful fraction of blood plasma in maintaining blood volume is albumin, which by virtue of its greater net charge and smaller molecular size, plays a greater role than the globulins in maintaining the normal osmotic relations of the blood and tissue fluids. Serum albumin is not only present in greater amounts than the other serum proteins, but also, because of its physicochemical properties, more stable and more soluble. These properties render it a theoretically ideal substitute for whole plasma in the treatment of shock.

This work has been made possible by the development in Cohn's laboratory of methods of fractionation of the plasma proteins whereby large-scale production is made feasible.[83] This depends on the substitution of alcohol—a cheap, commercial reagent that can be distilled off, condensed and used again—for ammonium sulfate as a precipitant. The precipitation is carried out in cellophane cylinders immersed in mixtures of alcohol and water, in which the concentration, pH and temperature are carefully controlled. The precipitate of albumin obtained can be readily dried, since it carries only a small volume of alcohol and water down with it, both of which are volatile at low pressures. Once dried, the material can be stored without precautions, and can be dissolved in buffered saline to any desired concentration when needed. Twenty-five per cent solutions of human albumin pass readily through a Seitz filter. The ease of sterilization and great solubility of this material make it possible to prepare highly concentrated solutions that take up very little space and are remarkably stable. The compactness and low viscosity of this human albumin preparation make it an exceedingly convenient form of substitute for whole blood, since it does not have to be reconstituted like dried plasma and is considerably less bulky. Clinical trials with

concentrated human albumin are under way, and it may play a very useful role as a therapeutic agent for the treatment of shock in emergencies.

Some of the earliest attempts at blood transfusion were made with heterologous blood, and usually resulted in fatal accidents. However, with the advent of plasma transfusion, interest has been revived in the use of heterologous plasma. Wangensteen and his associates[84] have used bovine plasma as a convenient form of plasma protein for parenteral administration to surgical patients unable to take food by mouth. His experiments have shown that bovine plasma can be administered in large doses to human beings, without fatal reactions. A number of moderate reactions occurred, but he successfully treated one patient in shock from an acute gastrointestinal hemorrhage. In following up Wangensteen's work, bovine plasma has been used as a source of purified albumin.[85] Work with this material is under way at present, but is still in the experimental phase. Immediate reactions are fairly well eliminated by the use of a sufficiently pure bovine albumin instead of whole plasma. The incidence of sensitization to beef products and serum disease with such a highly purified albumin is being carefully investigated.

Keys and his associates[86, 87] have recently noted their interest in this problem. They have separated albumin fractions from the serums of a number of animal species, but apparently have not been able to find any nonantigenic heterologous proteins for use in man.

It is too early to evaluate work of this type, but it represents an important experimental approach to the problem of providing cheap and readily available blood substitutes.

Other solutions have been proposed for the restoration of blood volume. Crystalloid solutions, such as saline, Ringer's solution and glucose, are of course extremely useful adjuncts to therapy, but their effect in shock is transient, because the fluid is not retained in the circulation. A number of workers have explored the possibility of using hemoglobin as a source of protein that would not only act to restore blood volume by virtue of its osmotic pressure, but would also be able to carry oxygen. Amberson[88] has shown that an animal deprived of most of its blood will remain alive for hours if it is infused with a hemoglobin-Ringer's solution. The trouble with hemoglobin as a blood substitute is that, although relatively innocuous, the molecule is treated as a foreign substance and is excreted to a considerable extent through the kidneys, where it may be precipitated as hematin in the tubules when an acid urine is secreted, with resulting kidney damage. This is thought to be the mechanism of anuria in transfusion reactions.[89–91] A number of workers have recently demonstrated that fairly large amounts of hemoglobin may be given intravenously to human beings without untoward results.[92,93] If measures to maintain an alkaline urine are adopted, such a hemoglobin-Ringer's solution has interesting possibilities, but it is hard to believe that a substance potentially dangerous in large amounts can replace the other proteins that are retained so much more effectively in the blood stream. Six per cent gum acacia in saline was introduced in World War I as a solution possessing the osmotic and viscous properties of blood.[94] Many of the results in shock were excellent.[95, 96] However, the evidence indicates that the gum is deposited in the liver cells, and the possibility of producing permanent liver damage cannot be dismissed too lightly when it is planned to use very large doses.[88–97] Taylor,[98] in Canada, has devised a solution of fish gelatin or isinglass, which seems to be relatively nonantigenic, and which in acute experiments in dogs was able to restore blood pressure after hemorrhage. Comparative studies[99] of various solutions in the therapy of acute hemorrhage in cats showed that gum acacia, hemoglobin-Ringer's solution, dilute plasma and serum were inferior to isotonic plasma and blood.

Another type of solution that may have properties of considerable value in the postoperative care of wounded patients is casein hydrolysate, which Whipple and his co-workers[100] and others[101, 102] have shown to be an extremely powerful stimulant to plasma-protein production when given intravenously. It should not be employed in the treatment of shock, but may be used in patients unable to take protein food by mouth. It consists of a mixture of amino acids and polypeptides derived from casein by enzymatic digestion.

From the practical standpoint, whole blood is unquestionably the ideal substance for the treatment of acute hemorrhage. Since it is not instantly available for use in the field and cannot be stored without refrigeration, plasma forms a very valuable substitute for immediate therapy, which can later be supplemented by blood transfusion when necessary.* Human albumin, by virtue of its convenient form, may turn out to play a valuable role in emergency treatment. Plasma and

*After removal of plasma, the remaining red-cell suspension may be used in the treatment of anemic patients.[103] The amount needed may be calculated from a modification of Marriott and Kekwick's formula[104]:

$$\frac{\text{Per cent rise in hemoglobin desired}}{100} \times \text{Normal blood volume (cc.)} = \text{Whole blood (cc.) required}$$

albumin are superior to blood in the treatment of burn shock. The use of gum acacia will probably be restricted to nephrotic edema, in which it may be more valuable than any form of plasma protein because it is not excreted in the urine.[105]

New Types of Traumatic Injuries

Blast Injuries

During World War I, a number of cases were observed in which death occurred without detectable injury. Such deaths from apparent concussion have occurred in the present war among people who were close to the points of explosion of large bombs. A considerable amount of experimental work has been done in England by Zuckerman[106] on the pathogenesis of this type of injury, and it has been found that pulmonary lesions are quite constant. These consist mainly of hemorrhages into the substance of the lung and the alveoli, with some bleb formation under the pleural surfaces, on which scattered petechial hemorrhages may be seen. Blood is usually found in the upper air passages, and x-ray films show various changes, including emphysema, mottled areas and patches of atelectasis. His investigations have shown that these injuries are produced by the pressure wave of the blast and not by the subsequent low pressure, as was first supposed. Covering the animals with a heavy layer of sponge rubber prevented the pulmonary lesions and protected the animals from the effects of the blast.

Two series of human cases have been reported. One group of patients known to be exposed to blasts at close range was studied from eight to ten days after the primary injury, but the findings were somewhat inconclusive.[107] The other group consisted of fatal cases in which post-mortem examination showed changes very similar to those found in the experimental animals.[108] In a few cases, lethal concentrations of carbon monoxide were demonstrated. The significance of this syndrome is that considerable hemorrhage may take place in the lungs without clinical symptoms. Therefore, patients known to have been exposed to blasts at close range should be kept under observation longer than their apparent condition warrants, since the x-ray and pathologic changes are always greatly in excess of the symptoms. The similarity of these cases to what has been referred to as traumatic pneumonia, occasionally observed in civilian practice, is striking. All observers agree that, although the pulmonary lesions may be important, they are not the cause of death, but merely one manifestation of the injury sustained by the organism.

Another syndrome of great interest, which has been described, so far as I know, for the first time during this war, is uremia complicating crush injuries, particularly of the extremities. A number of cases have been reported in the recent British literature of patients who sustained injuries of moderate or marked severity in which there was crushing of muscle tissue.[109–112] In these patients, after apparent recovery, oliguria developed, then anuria, edema of the crushed limb, azotemia and finally death on the sixth to eighth day after the injury or, in some cases, gradual recovery. The urine in such cases, when any was passed, was positive to benzidine, showed coarse brown granular casts, and was rather dark. Studies of the blood of these patients showed, in addition to a high figure for nonprotein nitrogen and a progressive acidosis, a marked rise in the concentration of serum potassium. The pathogenesis of this type of uremia was not understood at first, but Bywaters and Delory,[113] who described some of the first cases and who have studied the condition intensively, have shown that the pigment excreted in the urine that gives the benzidine reaction is not ordinary hemoglobin, but myohemoglobin. This pigment, of course, is derived from muscle, presumably in the injured area, and the likeliest explanation for the uremia seems to be the precipitation of myohematin in the renal tubules, producing anuria in the same manner as hematin after a hemolytic transfusion reaction. This suggests that the administration of fluids and alkali is advisable as early as possible for patients trapped in such a way that crushing injuries are incurred.

Control of Air-Borne Infections

Last year's review[114] mentioned briefly some of the possibilities in the control of air-borne infections, which constitute the most serious menace to health in crowded air-raid shelters. Respiratory diseases are the most difficult of any group of communicable diseases to control, and English and American workers have been studying this problem intensively in the past year. Their findings may prove of great value in the large military camps of the United States.

A recent report by Andrewes[115] summarizes his work and that of his colleagues. It points out that air-borne infection travels in three ways. The first is by coarse droplets, which are projected into the atmosphere by sneezing and coughing and

fall to the floor in a short time because of their size. Control of this form of spread is possible by adequate screening of individual patients and by proper masks, the most effective one that the English have found being made of a sheet of cellophane, which is impermeable to bacteria and viruses. It is worth pointing out that in the Boston Lying-in Hospital a mask consisting of a layer of nonabsorbent cotton folded into a layer of gauze has been used for some time. This utilizes the principle that bacteriologists have used for many years to exclude bacteria of the air from their cultures, and is highly effective. Since such a mask is cheap and can be discarded after use, it should replace the ordinary gauze mask used by most hospitals.

The second form of air-borne infection is by droplet nuclei. These are minute droplets, so small that they remain in suspension in the air for long periods. Each droplet nucleus may contain a few bacteria, and it is in this form that infection is borne about in the air through buildings, as has been demonstrated most clearly by the work of Wells and Wells.[116] Possibly, this type of infection can be controlled by the use of ultraviolet light. The English workers suggest that the air in shelters be drawn through a heavy muslin screen, which will serve as a filter for large droplets, then through a tunnel, in which ultraviolet lights are placed, and then ejected as sterile air into the room again. This is more effective and less expensive than placing ultraviolet lights about a room, as has been done in operating amphitheatres. Another method of combating droplet nuclei is by the use of aerosols. This development is due mainly to the studies of Trillat[117] and Twort et al.[118] Aerosols are antiseptic liquids nebulized in such a way as to form minute droplets much like the droplet nuclei mentioned above. These then remain suspended in the air for long periods as a fine mist, which is unnoticed by anyone present in the room. By such fine dispersion, a small amount of the liquid will fill quite a large room, and yet in each individual droplet the antiseptic solution can be kept at an effective level. Droplet nuclei and bacteria are attracted to the aerosol droplets, and the bacteria are killed by the antiseptics present in them. Hexylresorcinol in propylene glycol is the most effective known aerosol, but sodium hypochlorite can be used in 0.5 per cent solution very effectively without irritation to the mucous membranes. The British are experimenting with the use of these aerosols in the sterilization of shelters immediately before and after their occupation.

The third way in which bacteria are carried in the air is by dust. Droplets fall to the floor, the water evaporates, and the bacteria, particularly hemolytic streptococci and diphtheria and tubercle bacilli, may remain viable for long periods, to be swept up in the air with any disturbance. In this form, the organisms are resistant to ultraviolet light. Likewise, they are present on blankets, and it has been shown that the bacterial count of the air rises following bedmaking in a hospital ward. To control this type of infection, the British workers have found the application of oil to be most effective. Mineral oil is rubbed on the floors, and although a certain amount of luster is lost, sweeping of floors so treated will not throw bacteria up in the air. Hospital blankets can be treated in such a way with mineral oil in naphthalene or some similar solvent that the blankets appear perfectly normal. However, they retain about 3 per cent by weight of oil, and this suffices to trap bacteria.

* * *

This brief report on progress in military medicine shows that the necessities of war have served as a stimulus to research that may have a vital bearing on medical practice and the prevention of sickness in peace as well as in war.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27361

PRESENTATION OF CASE

First Admission. A sixty-two-year-old retired saloon keeper entered the hospital for study.

The patient was well until six years before admission, when he began to suffer from rather severe, steady, upper abdominal pain accompanied by a tremendous swelling of his abdomen and swelling of the feet. He remained in bed for fourteen months, and many abdominal paracenteses were performed by his physician, who withdrew as much as 10 liters of fluid at one time. Then, the symptoms cleared, and he went back to work, although he did not feel entirely well. During the twelve years preceding this illness, the patient had consumed a great deal of beer and a pint of whiskey a day. He abstained during his illness, but soon began again. One day, about ten months before admission, the patient was seized with a sudden desire to move his bowels, and on doing so found that he had passed a huge quantity of dark blood. Almost immediately, he vomited a cupful of blood and collapsed to the floor. He remained in bed for one week, exhausted, but otherwise symptomless, and then returned to work. Melena and hematemesis again occurred four months later.

Five months before admission, the patient noticed that his feet were swollen. Two months later, when the swelling was beginning to subside, he was seized with severe fleeting pains in his knees and ankles, and these joints became red, swollen and so tender that he was unable to walk or rest the bedclothes on them. The pain remained in a joint for a week and then passed to another, so that at the time of admission the hips, ankles, great toes, left elbow and wrist, and the joints of both hands had been involved. The patient stated that he had been troubled with similar pains in his right great toe for many years, the attacks occurring about once in six months and lasting for a week. Furthermore, he complained of a nocturia of three times and generalized pruritus for the previous year. He had lost 20 pounds in six years.

The past illnesses were irrelevant.

On examination, the patient was well developed, moderately well nourished, pale and slightly short of breath. Clotted blood was found in the nose and posterior pharynx. Dilated veins were present over the chest and abdomen. The lungs were clear, the heart slightly enlarged, and the sounds distant; the blood pressure was 230 systolic, 118 diastolic. The abdomen was swollen and tense; a fluid wave and shifting dullness could be demonstrated; and a smooth, rounded, nontender liver edge was palpable three fingerbreadths below the costal margin. The left hand and wrist were slightly swollen, and the skin over the dorsum of the hands was shiny.

The temperature, pulse and respirations were normal.

The urine showed a ++++ test for albumin and a pH of 5; the sediment contained occasional red and white cells and a rare hyaline cast. Urine concentration tests showed a specific gravity of 1.011, and a phenolsulfonephthalein test showed no excretion of the dye in two hours.

The blood showed a red-cell count of 3,000,000 with a hemoglobin of 8.5 gm. (photoelectric-cell technic), and a white-cell count of 8800 with 79 per cent polymorphonuclears, 11 per cent lymphocytes, 4 per cent monocytes, 5 per cent eosinophils and 1 per cent basophils. A platelet count was 204,000, the bleeding time 3 minutes, the clotting time 14 minutes, the sedimentation rate 0.2 mm. per minute, and the hematocrit reading 23 per cent. The nonprotein nitrogen of the blood serum was 130 mg. per 100 cc., the uric acid 10.3 mg. and the protein 6.7 gm. The serum van den Bergh was normal. The formol-gel test was positive, and a bromsulfalein test showed 0 to 5 per cent retention. The prothrombin time was 16 seconds (normal). The venous pressure was equivalent to 35 mm. of water, and the vital capacity was 2400 cc. A prostatic smear was negative for the gonococcus.

A gastrointestinal series showed a wide esophagus, but no varices; there was a small hiatus hernia. The stomach showed no evidence of disease; the duodenal cap was narrow at the apex, but no crater was seen. X-ray examination of the various joints showed atrophy of the bones of the hands, with some ulnar deviation in the fingers of the metacarpal joints. Small defects of the joint surfaces were present in several interphalangeal joints. In the feet, there were small defects in the first right metatarsophalangeal joint, with secondary degenerative changes. Degenerative changes were also present in the corresponding joint on the left side. The shoulder joints, cervical spine, knees and ankles were normal.

An electrocardiogram showed normal rhythm

at a rate of 75, with a PR interval of 0.18 second; S_1 and S_2 were prominent, and Q_3 measured 5 mm.

During hospitalization, the patient gradually improved, although he was very drowsy, and from time to time various joints became painful, tender and occasionally hot and swollen. Thus, the wrists, elbows, cervical spine, knees, ankles and toes were involved, but the pain subsided within a few days. One week after admission, the blood calcium was 6.3 mg., and the phosphorus 9.3 mg. per 100 cc.; the phosphatase was 4.1 Bodansky units, and the carbon dioxide combining power 12.9 milliequiv. and the chlorides 108.0 milliequiv. per liter. Sodium citrate and aluminum hydroxide were given, and eight days later the phosphorus was 6.2 mg. and the calcium still 6.1 mg. per 100 cc.; the uric acid remained around 9 mg., and the nonprotein nitrogen was 110 mg. per 100 cc.

One month after admission, the calcium was 6.0 mg. and the phosphorus 4.7 mg. per 100 cc.; the carbon dioxide combining power was 26.1 milliequiv., and the chlorides 103.6 milliequiv. per liter. Gradually, the patient's breath became less uremic, and the nonprotein nitrogen fell to 85 mg. per 100 cc. About this time, punctate hemorrhages occurred over both shins, and ankle edema was present. A tourniquet test showed 40 to 50 petechiae per inch; the vitamin C was 1.3 mg. per 100 cc., and the prothrombin time and platelets were normal.

Six weeks after admission, the patient's gastric and joint symptoms had disappeared, and he was brighter and stronger. Calcium gluconate was added to the regimen, and at the time of discharge on the thirty-ninth hospital day the blood calcium was 8.2 mg. and the phosphorus 5.1 mg. per 100 cc.; the total base was 150.0 milliequiv. per liter, and the sodium 140.5 milliequiv.

Final Admission (two weeks later). The patient carried on without mishap until five days before admission, when he was seized with a sudden precordial pain without radiation, which was so severe that he thought he was going to die. Since this attack, the duration of which was not stated, he had suffered from shortness of breath, orthopnea and weakness. On the day before admission, the patient came to the Emergency Ward, where examination was the same as at the time of discharge, with the following additions. There was orthopnea, a cardiac gallop rhythm, with a blood pressure of 220 systolic, 110 diastolic, and edema of the feet. On the following day, the patient again suffered a severe squeezing pain across the upper chest, without radiation. This pain gradually subsided, and was followed by cyanosis, sweating and acute pulmonary edema.

On examination, the patient was lying propped up in bed in acute respiratory distress and wheezing, with quantities of mucus in the throat. There was venous distention to the angle of the jaw. The left border of the heart was at the anterior axillary line; gallop rhythm was present, and the blood pressure was 210 systolic, 106 diastolic. The lungs were filled with coarse rales, rhonchi and groans.

The temperature was normal, the pulse 124, and the respirations 30.

The urine showed a ++++ test for albumin. The nonprotein nitrogen of the blood serum was 110 mg., the uric acid 8.5 mg., the calcium 9.0 mg. and the phosphorus 7.3 mg. per 100 cc.; the chlorides were 111.4 milliequiv., and the carbon dioxide combining power 15.6 milliequiv. per liter. The sedimentation rate was 0.9 mm. per minute, the venous pressure 132.

An electrocardiogram showed normal rhythm, with a rate of 110 and a PR interval of 0.17 second; S_1 and S_2 were slightly prominent, and T_4 was low. Five days later, T_1 was diphasic, and T_4 showed late inversion. Four days after this tracing, there was little change.

Although the patient's lungs gradually cleared, peripheral edema increased, ascites developed, and blood was noted in the stools. One week after admission, he became disorientated and shortly afterward stuporous. Death occurred on the twenty-third hospital day.

Differential Diagnosis

Dr. Bernard M. Jacobson: The swelling of the feet five months before admission is a surprising finding. We wonder why the patient did not have continuous swelling most of the time during the preceding year. I should suggest that the story as told or as recorded is not correct, because if his ankles, knees and other joints were red, swollen and tender, and he could not rest the bedclothes on them, the pains were not fleeting.

I do not believe we can escape the early conclusion that this man had portal decompensation in the course of alcoholic cirrhosis of the liver. I cannot imagine any other disease that would cause abdominal swelling and such massive ascites over such a long period. On the basis of the physical findings, there is no evidence of heart failure or renal failure as a cause of the abdominal fluid. Furthermore, we know that the patient had a good background for a diagnosis of alcoholic cirrhosis, and also for a probable diagnosis of polyarticular rheumatism.

We are not told on physical examination whether he did or did not have any tophi. Regardless of this fact, I think the diagnosis of gout is the most likely one. The patient had recurrent attacks in one or another of the big toes, presumably in the metatarsophalangeal joint. It is interesting that, as the swelling of the feet subsided, the gout became more noticeable; this is proof of the well-known fact that an attack of gout can be provoked by induced or spontaneous diuresis. It is extremely unlikely that the joint disturbances could be due to infectious or rheumatoid arthritis, which, over a period of years, would most certainly have resulted in joint disability between attacks. The entire clinical picture during the five months previous to entry is perfectly compatible with gout.

It is interesting that the patient was pale and slightly short of breath, with blood in his nose, and some explanation of that should be made. The urine showed a ++++ test for albumin. The urine concentration test showed a specific gravity of 1.011, and a phenolsulfonephthalein test showed no excretion of the dye in two hours. That is the first definite clue that there was something very wrong with the kidneys. The blood picture showed a moderate normochromic anemia. So far as the diagnosis of gout goes, the uric acid level of 10.3 mg. per 100 cc. is of no help, because it is elevated in every case of renal insufficiency with marked nitrogenous retention. Is the uric acid more elevated in relation to the nonprotein nitrogen in the presence of both gout and uremia? I do not know, but I think so. The formol-gel test is positive in most cases of cirrhosis of the liver. I am a little disturbed that the liver function, as measured by dye excretion, was so good, and that the serum van den Bergh was normal. I should expect, in a typical case of portal cirrhosis, a slight degree of dye retention. Nevertheless, that does not mitigate against the diagnosis of portal decompensation. Of course, in any person with cirrhosis of the liver who vomits or passes blood, our first thought concerns varices in the esophagus. On the other hand, the fact that the x-ray film did not show them does not rule them out. We know that in alcoholism there are other causes for vomiting; one that might result in a severe hemorrhage and still not be seen by x-ray is severe gastritis. So far, we have no evidence for or against that diagnosis.

X-ray examination showed a fair degree of narrowing of the joint spaces in the feet, with a certain amount of atrophy. The hands showed little except degenerative changes. In other words, the x-ray picture was compatible with a diagnosis of gout, that is, it showed very little bone or joint change. On the other hand, even if the findings were more marked than these and even if they simulated rheumatoid arthritis more seriously, they would be compatible with gout, as we have seen in quite a few cases in this hospital.

The electrocardiogram was not significantly abnormal.

According to the record, the cervical spine was involved. That is disturbing, if true, because by and large it is extremely rare for acute gout to involve any part of the cervical, dorsal or lumbar spine. I rather imagine that this probably represents acute tenosynovitis in the ligaments or tendons of the neck.

There was a very marked degree of hypocalcemia, high phosphorus retention due to kidney insufficiency, and marked acidosis, with only 50 per cent of the normal carbon dioxide combining power. One would certainly expect a patient with a calcium of 6.3 mg. per 100 cc. to have a positive Chvostek's sign. I rather imagine that this patient did not have it because of the high degree of acidosis.

The sodium citrate and aluminum hydroxide were given presumably to try to normalize the calcium-phosphorus metabolism; however, eight days later it was about the same. We are not told whether the patient received specific therapy for the gout, such as colchicine.

We are now faced with the terminal event, and we are unable to obtain further information about the fundamental diagnosis. In a person of sixty-two with hypertension and gout, I should say the most likely thing would be a severe degree of nephrosclerosis, a terminal vascular disease in the kidneys. There is nothing in the past history to suggest acute or subacute glomerulonephritis, any infectious type of nephritis, pyelonephritis or any other type of renal disease. I say "with gout" because renal vascular disease is commoner in people with long-standing gout than in other people.

Is this a gouty nephritis? I think it has been decided that we do not know exactly what gouty nephritis is. True, some people at autopsy show high degrees of vascular change and some uric acid crystals in or around the tubules. I should say that if this attack was acute it was not due to a primary type of renal disease.

In the record of the last admission, there is a definite change in electrocardiographic findings from what was previously recorded—a low T_1 five days after acute chest pain. Five days later, T_1 was diphasic. In view of the history, the

electrocardiographic findings, the clinical findings and the acute cardiac decompensation, there can be little doubt that there was coronary occlusion, with an infarct of the anterior type. We are not told very much at the time of the last admission about the amount of fluid in the abdomen or the feel of the liver after paracentesis. There is no question that the terminal event was coronary occlusion and cardiac failure.

He also had blood in the stools as a terminal event. Whether that was bleeding from esophageal varices or gastritis or possibly from the hiatus hernia, which is rather unlikely, or a uremic colitis, it is impossible to say.

I have mentioned most of the differential diagnoses, and I sum up the list of probable diagnoses as follows: gout, portal cirrhosis, arteriosclerosis, hypertension, nephrosclerosis with uremia, coronary occlusion with cardiac failure, and questionable gastritis or esophageal varices as the cause of the bleeding. I should like to add that I am still disturbed by the fact that the liver is reported to have felt smooth and round. I do not recall ever having seen a case of portal cirrhosis in which the liver felt smooth.

Dr. Alfred Kranes: Do you not think that, clinically, the liver is always smooth in portal cirrhosis?

Dr. Jacobson: I think it is irregular.

Dr. Kranes: Do you think one can always feel the small nodes clinically?

Dr. Jacobson: No; I mean after paracentesis, when the abdomen is flat.

Dr. Tracy B. Mallory: I should be inclined to agree with Dr. Kranes. I am skeptical if anyone feels irregularities in a cirrhotic liver. At the stage when the liver is big enough to be felt, the granules that are present are particularly small, and it seems to me that it would be impossible to feel them.

Clinical Diagnoses

Gout.
Chronic glomerulonephritis.
Uremia.
Cirrhosis of liver.

Dr. Jacobson's Diagnoses

Portal cirrhosis.
Hypertension.
Generalized arteriosclerosis.
Nephrosclerosis.
Uremia.
Gout.
Coronary occlusion.
Cardiac failure.
Gastritis (?) or esophageal varices (?).

Anatomical Diagnoses

Gout.
Alcoholic cirrhosis of the liver.
Splenomegaly.
Esophageal varices.
Chronic vascular nephritis.
Uremic colitis.
Hypertrophy of the heart.
Bronchopneumonia.

Pathological Discussion

Dr. Mallory: At the post-mortem examination, no tophi were discovered. Many of the joints showed extensive urate deposits. About 5 liters of ascitic fluid was found.

The liver was larger than normal, and possibly a reason for the smoothness was the fact that it was rather markedly frosted with a heavy layer of white fibrous tissue, so that even a 1-cm. nodule certainly could not have been felt. The cut surface of the liver showed a marked increase in fibrous tissue, complete destruction of the architecture and innumerable little granules of encapsulated liver tissue; the largest of them was 3 mm. in diameter, however, and the vast majority were 1 or 2 mm. Microscopically, it was typical of an alcoholic cirrhosis. The spleen was somewhat enlarged, weighing 350 gm., and also showed a frosted capsule. The esophagus showed very evident varices. It is surprising that they were not shown by the x-ray studies, which often show varices that we have difficulty in finding at autopsy. None of them, so far as we could make out, had bled recently. At any rate, there was no ruptured varix at the time of death. There was no marked grade of gastritis, but the colon showed a very severe hemorrhagic colitis and was filled with a bloody mucous fluid. I think the terminal hemorrhage from the bowel almost certainly came from the colon rather than the esophagus. Some of the earlier episodes of hematemesis probably did come from the esophagus. The colitis was not specific in character and corresponded to what we usually call "uremic colitis."

The heart was hypertrophied, but we could find no infarct, and the coronary arteries were very good, not even markedly narrowed; there was no pericarditis. The lungs were normal.

The kidneys were small, the pair weighing 220 gm. The gross appearance was that of nephrosclerosis. Just after the autopsy, some pieces of kidney were examined under the dissecting microscope, and it was thought that some uric acid crystals could be identified at the time. Later, sections of alcohol-fixed material stained specifically for uric acid failed to show it, so that I think

that was an overenthusiastic observation. If you try to pin me down as to what kind of renal involvement this patient had, I think I should have to say nephrosclerosis, although it is not quite the ordinary benign vascular nephritis. I have never been able to convince myself that there is a specific form of gouty nephritis, but gouty kidneys generally look a little unusual, without any sufficiently specific characteristics for one to recognize them.

CASE 27362

Presentation of Case

A forty-year-old married Italian chef was admitted to the hospital complaining of pain in the right arm and shoulder of five months' duration.

Five months prior to entry, the patient noted the onset of sharp, sticking pain in the right shoulder, which was intermittent, lasted about ten minutes, and was usually precipitated by motion. There was a steady daily increase in its frequency and severity until three months before entry, when it became essentially constant. At this time, it radiated down the right arm to the hand. One month later, two small painful nodules the size of the end of the little finger appeared along the ulnar aspect of the right forearm, near the wrist. A painless one had developed on the flexor surface of the right forearm five years previously. All these nodules were freely movable and tender to pressure. Simultaneously with the appearance of the nodules, the patient developed a burning, sharp pain, which radiated down the ulnar aspect of the forearm, hand and fourth and fifth fingers. Weakness of the first, second and third fingers followed, with inability to flex the thumb and index finger completely. Ten weeks before admission, the right eyelid began to droop. The weight had decreased 10 to 15 pounds within three months.

Six or seven years before entry, the patient had jaundice, which lasted for six months and was unaccompanied by fever or prostration. He drank excessively of wine and whiskey until the onset of his present illness, when his physician ordered him to stop.

Physical examination showed a well-developed, poorly nourished man in considerable pain, who carried his right shoulder high; his arm was splinted. There was moderate ptosis of the right eyelid and slight enophthalmos. Perspiration was decreased on the right side of the face. The pupils reacted sluggishly to light and accommodation. A narrow pigmented area measuring 7 by 2 cm. was seen on the back of the neck, just to the left of the mid-line. The mouth showed pyorrhea, and the uvula was deviated to the right. There was slight atrophy of the right arm and hand; the grip was very weak. Reflexes in the right arm were diminished. A narrow band of anesthesia was outlined over the triceps muscle and the ulnar areas of the forearm and fourth and fifth fingers. Over the lower left chest wall just lateral to the spine was a slightly elevated area measuring 4 by 4 cm. It was dull to percussion, and breath sounds were diminished beneath it. Transient crackling rales around it disappeared on coughing. The right apex was dull to percussion. Examination of the heart was negative. A fixed, firm, slightly tender mass 12 cm. in width was palpated in the epigastrium. There were two subcutaneous nodules on the right forearm, and a movable, firm subcutaneous nodule over the lower portion of the triceps muscle of the right upper arm. The other extremities were normal. The spine showed moderate tenderness to pressure over the sixth cervical vertebra.

The temperature was 97°F., the pulse 90, and the respirations 15.

Examination of the urine was negative. The blood showed a red-cell count of 6,020,000 with 104 per cent hemoglobin, and a white-cell count of 7000 with 74 per cent polymorphonuclears, 16 per cent lymphocytes, 6 per cent mononuclears, 3 per cent eosinophils and 1 per cent basophils. Four stool examinations were guaiac negative. A blood Hinton reaction was negative; a serum van den Bergh was normal, indirect. A bromsulfalein test of liver function showed 0 to 5 per cent retention; a Takata-Ara test was positive. A lumbar puncture showed normal dynamics. There were no cells in the spinal fluid; the total protein was 32 mg. per 100 cc., the gold-sol curve 0121000000, and the Wassermann reaction negative.

X-ray films of the skull and right shoulder were negative. There was destruction of 2.5 cm. of the vertebral end of the first rib on the right side, and complete destruction of the transverse process of the first dorsal vertebra. Chest films showed a soft-tissue mass depressing the right apex. There were two small rounded areas of decreased density overlying the ninth rib posteriorly on the right, and a questionable round area of increased density in the third intercostal space on the left. Lateral films showed a pathologic fracture of the spinous process of the first dorsal vertebra. A gastrointestinal series was negative, except that the stomach in the region of its angle was displaced downward. The right lobe of the liver seemed

slightly smaller than normal. The spleen was questionably enlarged. The right kidney appeared normal; the left was enlarged, but showed no visible tumor.

On the third hospital day, a biopsy of one of the nodules of the right upper arm showed a lipoma. The liver edge and spleen were palpated, neither being nodular. The epigastric mass on the following day seemed by palpation to be part of a large mass in the left flank. The red-cell count was 7,100,000, with 110 per cent hemoglobin. On the seventh hospital day, the oxygen capacity of the blood was 20.7 per cent, the cell volume 53.2 per cent, and the hemoglobin concentration 17.4 milliequiv. per liter. The symptoms of pain had been increasing, and the patient complained of weakness in the legs and difficulty in starting the urinary stream. The knee and ankle jerks on the right were spastic, with clonus and equivocal Babinski signs. They were normal on the left. There was hypesthesia to light touch and pinprick over the left lower extremity, and hypesthesia to pinprick over the left trunk. There was diminished vibratory sensation on the right below the clavicle.

On the eleventh hospital day, an intravenous pyelogram showed a normal kidney pelvis on the right. On the left, there was marked separation of the calyxes, the upper and lower calyxes being pressed apart and the lower calyxes markedly expanded. The spine showed increased destruction of the seventh cervical and first dorsal vertebras. Apparent metastatic nodules were present in the lower portion of the left lung, and a large mass was seen in the region of the destruction of the eleventh rib on the left side.

The patient rapidly failed, and was aroused with difficulty. The temperature, pulse and respirations had remained unchanged since entry, but on the eleventh hospital day the temperature gradually rose to 106°F. rectally; the patient died early on the twelfth day.

Differential Diagnosis

Dr. Earle M. Chapman: This patient apparently died because of widespread tumor, the origin and type of which are uncertain. However, I can offer certain clinical speculations about its nature. In the first place, I think that none of us are misled by the story that painless nodules had been noted on the arm five years before entry into the hospital. We can accept this statement and associate it with the one biopsy diagnosis that we have — lipoma.

Another fact, perhaps dissociated from the cause of death, is that the patient was a heavy drinker and had damaged his liver some six or seven years before entry. In the present findings are several bits of evidence to suggest that he continued to have a moderate degree of portal cirrhosis: the liver was palpable, but by x-ray study the right lobe appeared small; and the spleen was palpated and enlarged. This is substantiated by the positive Takata-Ara test, which, according to Dr. Clark W. Heath at the Boston City Hospital, is always of more value as a positive than a negative test. With only 0 to 5 per cent retention of bromsulfalein, we cannot assume any great degree of liver failure. Tests of liver function have been justly criticized for their failure to indicate minimal disease, but Deutsch[1] has recently modified the bromsulfalein test and applied to it the same modification that I made of the phthalein test of kidney function.[2] He also used the fractional method by obtaining serum five and fifteen minutes after the injection of the dye and found that this often reflects a degree of liver injury before the usual one-hour test. Here would have been an ideal case in which to apply his new method.

Returning to the main problem of this patient's tumor, I think we can agree that it was rapidly growing and apparently had an affinity for lung and bone tissue, which, in turn, suggests that oxygen exchange in these bony or marrow areas may be greater than we have estimated. X-ray study confirmed the presence of destructive (osteolytic) processes in the first rib, the first dorsal and later the seventh cervical vertebra. Tenderness was present over the last — a simple sign of its involvement. Several metastases were seen in the lung fields. To me, the description of the depressed right apex does not indicate the so-called "Pancoast tumor." A Horner's syndrome, which can be produced by pressure from any tumor in this region of the superior sulcus, was present on the right, and the later signs suggest that the patient finally had an intracranial lesion.

But where did this tumor begin? The pigmented area, 7 by 2 cm., on the back of the neck might well have been the origin of a melanotic sarcoma. However, I am inclined to believe that the tender abdominal mass was related to the distortion of the left kidney pelvis, and since this was by far the largest tumor, — hence, presumably, the oldest, — it may well have been the origin of the trouble. In people of this age, the kidney tumor that metastasizes to bones and lungs is hypernephroma. Perhaps it was this tumor in the lungs that interfered with oxygen exchange and

so caused the mild but definite polycythemia, more cells being needed to carry the same amount of oxygen from the limited lung surfaces. It is amazing that the tumor grew to this size and failed to cause urinary changes.

Clinical Diagnosis

Hypernephroma, with widespread metastases.

Dr. Chapman's Diagnoses

Portal cirrhosis, moderate.
Multiple lipomas.
Hypernephroma, left kidney, with widespread metastases.
Polycythemia, secondary to obliteration of the lung fields.

Anatomical Diagnoses

Portal cirrhosis of the liver.
Hepatoma, with metastases to lungs, bone and left adrenal gland.
Tumor thrombi of hepatic vein and inferior vena cava.
Splenomegaly, secondary to portal obstruction.
? Polycythemia vera.

Pathological Discussion

Dr. Tracy B. Mallory: This was obviously a very puzzling case from the diagnostic point of view. There were many leads, but each of them seemed to be contradicted by some other finding, or to be absolutely without confirmatory support. It is extraordinary, for example, to find a man dying of metastatic malignant disease with a polycythemia instead of an anemia. The Pancoast syndrome suggested a primary bronchiogenic carcinoma, but the x-ray examination showed clearly that the tumor was outside the lungs. The pyelogram suggested hypernephroma, but the urine was normal and the history of alcoholism and the suspicious evidences of cirrhosis seemed simply a complicating factor. The clinicians on the wards reasoned essentially as Dr. Chapman did, and likewise came to the conclusion that hypernephroma was the best bet. As a matter of fact, the most important lead in the record was the history of chronic alcoholism, for the patient had a cirrhosis and he had that by no means uncommon complication of cirrhosis, a primary liver-cell carcinoma or hepatoma. The roentgenologist was correct in his opinion that the right lobe of the liver was smaller than normal, but the left lobe was more than correspondingly enlarged and almost completely replaced with tumor. As these hepatomas characteristically do, the tumor had invaded and grown along the hepatic vein up to the vena cava, into which a nubbin of tumor thrombus that narrowed it by a quarter of its cross-sectional area had projected.

It had metastasized extensively, and there were numerous small tumor nodules in the lungs. The tumor responsible for the Horner's syndrome was metastasis to the seventh cervical vertebra, which had grown forward and downward to displace the apex of the lung. It did not invade the brachial plexus and must have produced its effect by pressure only. Another large metastasis had completely replaced the left adrenal gland, and it must have been adhesions from this tumor mass that were responsible for the deformity of the left renal pelvis. The epigastric mass was, I imagine, mostly the left lobe of the liver, although it is possible that the adrenal tumor may also have been felt. The spleen was greatly enlarged, weighing 800 gm., but they apparently were able to dissociate this from the epigastric mass.

I am entirely at a loss to explain the polycythemia. It was certainly greater than could be explained merely by dehydration. The bone marrow showed, besides the major metastatic lesions, recognized by the roentgenologist, multiple miliary metastases, and therefore one would have expected an anemia. The portion not involved by tumor showed an extreme grade of erythrocytic hyperplasia, and was consistent with but hardly diagnostic of a polycythemia vera. I had hoped that the spleen might help us make such a diagnosis, but it showed only the marked sinusoidal engorgement and the fibrosis of the pulp characteristic of long-standing portal congestion, such as is seen with cirrhosis of the liver and in the so-called "Banti's syndrome." Dr. Chapman's suggestion of a secondary polycythemia based on pulmonary insufficiency is interesting, but I am unable to agree with him. The extent of metastatic involvement of the lungs was not nearly so great as we frequently see, and I cannot remember ever to have seen a secondary functional polycythemia based on neoplastic replacement of pulmonary tissue.

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POSTGRADUATE MEDICAL EDUCATION

The 1940 report of the Commission on Graduate Medical Education* devoted more of its space to the discussion of internships, residencies and specialties than it did to the needs of the practicing physician. The commission is aware of the serious problems involved in this wider field, however, for it acknowledged the need of postgraduate education for family doctors from many points of view. The report stated, "The time is now ripe for the development of broad standards of educational content of postgraduate work, standards that will emphasize objectives and stimulate higher achievement without inhibiting widespread experimentation with means and methods." Particular attention should therefore be paid to an article appearing in this issue of the *Journal*. If the time is ripe, it appears that the program of Tufts College Medical School for postgraduate medical education offers some of the "means and methods."

Three years of experimentation in this field are worth recording. How much of the present program will be continued and how much will need to be readapted, it is impossible to say. The program as a whole has behind it a broad conception of the problem. It visualizes a medical service that is not rendered by the physician alone, but by a group of people and facilities under the direction of the physician. If the physician wants an electrocardiogram, he must have the facilities for obtaining it, and if he cannot fully understand its implications, he must have help in its interpretation. If he is taught what the clinical laboratory can do for him today, a laboratory and a technician must be made available. If he understands and appreciates the possibilities of modern x-ray technic, proper apparatus must be provided. Much of the discouragement of the alert practicing physician comes from his inability to make his own diagnostic knowledge effective through lack of personnel or material, or both. An initial attempt to supply these deficiencies by paralleling postgraduate education with an affiliated system of regional and community hospitals, including all the usual ancillary activities and services, has been made, apparently with a considerable measure of success. The Bingham Associates Fund appears to have made an auspicious entrance into the field of medical education at Tufts.

*Commission on Graduate Medical Education. *Graduate Medical Education*. 304 pp. Chicago: University of Chicago Press, 1940. P. 200.

THE TREATMENT OF TRAUMATIC SHOCK

Although the problem of shock has continued to challenge investigators since World War I, the present war has given a great impetus to research in this field. Since shock is a state that is difficult to define, and can come about in a number of ways, it is small wonder that the prob-

lem of its pathogenesis is not settled. However, great progress has been made, and intelligent therapy is now possible, partly because of better understanding of the underlying pathologic physiology of the condition and partly because of the development of intravenous therapy with blood, plasma and crystalloid solutions. Stead,[1] in a recent review, has shown that our understanding of traumatic shock is considerably better than that of medical shock, and treatment more efficacious. An important consideration in traumatic shock is its early recognition. As Dunphy[2] points out, a patient who has lost a considerable volume of blood from hemorrhage may not appear different from a normal person, but cannot tolerate a further loss of a few hundred cubic centimeters of blood, which would not affect a normal person. In other words, the patient is compensated, but like a compensated cardiac patient, has a very low margin of safety. In some patients, incipient shock may be recognized by an increasing concentration of the blood. In others, it must be recognized by noting the degree of hemorrhage, sweating or other loss of fluid. This is particularly true in surgical operations, in which the loss of blood may be considerable, without any obvious gross hemorrhage.

Wound shock is brought about by neurogenic mechanisms due to pain, fright and concussion, and by hematogenic mechanisms due to hemorrhage and oozing of plasma into injured areas. That toxic substances absorbed from the injured tissue play a role is possible but has not been absolutely proved. In any case, the patient usually exhibits the signs of peripheral circulatory failure: feeble thready pulse, low pulse pressure, pallor and, frequently, hemoconcentration and low blood pressure. Since the volume of circulating blood falls from loss of blood and plasma, and since peripheral vasoconstriction increases, tissue anoxia results, with a further increase in capillary permeability and a consequent additional loss of plasma.

The treatment of traumatic shock depends on attacking the mechanism at fault. The use of drugs alone is to be decried. Morphine has much to offer in diminishing pain and anxiety, but vasoconstrictor drugs, which may be quite useful in vasomotor collapse, such as that which occurs with spinal anesthesia, are contraindicated in traumatic shock, in which vasoconstriction — as evidenced by pallor, sweating, cool skin and thready pulse — is already present. Oxygen may be useful in combating general capillary damage. The use of adrenocortical hormone and synthetic desoxycorticosterone has been widely discussed, but little is known of their value in shock. Controlled fluid therapy is the sheet anchor of treatment and prophylaxis of traumatic shock,[3] as pointed out in the progress report in this issue of the *Journal*. To quote Blalock and Mason[4]:

> In the treatment of traumatic shock the primary objective is the restoration of a blood volume, which has been reduced in consequence of hemorrhage, loss of plasma locally at the site of injury, or generally as a result of increased capillary permeability. Infusion of crystalloid solutions only transiently increases the blood volume and may, eventually, still further reduce it. Only whole blood or plasma may safely, effectively, and permanently restore the volume of the circulation, and of these plasma is preferable, because a unit volume supplies more osmotically active protein than does whole blood. The latter usually is essential only in the presence of profound anemia.

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3. Drew, C. R., Scudder, J., and Papps, J. Controlled fluid therapy: with hematocrit, specific gravity, and plasma protein determination. *Surg., Gynec. & Obst.* **70**:859-867, 1940.
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MEDICAL EPONYM

Kahler's Disease

Professor Otto Kahler (1849–1893), of Prague, first directed attention to the association between Bence-Jones proteinuria and multiple myeloma in a paper, "Zur Symptomatologie des multiplen Myeloms: Beobachtung von Albumosurie [On the Symptomatology of Multiple Myeloma: Observation on Albumosuria]," that appeared in the *Prager medizinische Wochenschrift* (**14**:33–35, 45–49, 1889). After describing his own case and adducing evidence that the diagnoses of osteomalacia made in earlier reported cases of albumosuria were incorrect, he says:

> In the above review, I believe I have done no violence to the facts, and accordingly feel justified in rais-

ing the question whether there was not in both these previous cases of marked albumosuria a multiple primary lymphosarcoma of the bone marrow exactly as in our case.

If I further venture with at least some degree of probability to answer this question in the affirmative, I may justifiably designate the marked albumosuria, which was noted in three similar cases, a frequently encountered symptom of this disease of the bone marrow.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Death of Undetermined Origin, Following Forceps Delivery of a Hydrocephalic Fetus

A nineteen-year-old primipara had had no prenatal care and was not seen until she arrived in the hospital in labor. The blood pressure was 180 systolic; albumin was present in the urine; and there was marked edema of the extremities, of unspecified duration.

The past history was noncontributory. Examination revealed that the fetus was hydrocephalic, and after fourteen hours of labor, a forceps delivery was performed following a craniotomy. The hospital record states that the patient died suddenly on the fifth day.

Comment. This is another fatality in a patient who had had no prenatal care, yet the death can in no way be attributed to its lack. Had the patient been under intelligent observation, the hypertension and albuminuria would undoubtedly have been recognized before she entered the hospital, and would have been treated earlier; however, it does not seem that toxemia entered into the death, since the history reveals nothing that suggests anuria or a convulsion. The record does not state whether the blood pressure came down after delivery. It is possible that it remained high, and that the sudden death might have been due to a cerebral hemorrhage, although the history is more suggestive of a death from embolus.

Adequate prenatal care would have made the diagnosis of hydrocephalus possible before labor, but the patient would have been treated no differently. When it is known that a hydrocephalus exists, labor is allowed to proceed to full dilatation, and craniotomy is then performed. That was done in this case. There is nothing in the record to suggest that the puerperium was complicated by fever. If it had been, the embolus at five days might have resulted from a pelvic phlebitis. Emboli occur at any time following a normal labor, and when there has been no febrile disturbance or recognizable phlebitis, they must be regarded as nonpreventable.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, *Secretary*, 330 Dartmouth Street, Boston.

DEATHS

ALEXANDER — Thomas B. Alexander, M.D., of Scituate, died August 28. He was in his sixty-sixth year.

A native of North Grantham, New Hampshire, he received his degree from Baltimore Medical College in 1901. He was a fellow of the Massachusetts Medical Society and the American Medical Association, and was a former president of the Norfolk South District Medical Society.

He is survived by his widow and two daughters.

GAFNEY — Harry D. Gafney, M.D., of Ware, died July 31. He was in his sixty-third year.

Dr. Gafney received his degree from Harvard Medical School in 1903. He was a former member of the Massachusetts Medical Society.

His widow and two sons survive him.

GIBBS — Howard A. Gibbs, M.D., of Blandford, died August 10. He was in his eighty-third year.

Dr. Gibbs received his degree from Boston University School of Medicine in 1882. He was a former member of the Massachusetts Medical Society.

He is survived by his widow, six sons and six daughters.

POPE — Frank F. Pope, M.D., of Ashby, died August 27. He was in his eighty-third year.

Dr. Pope received his degree from Dartmouth Medical School in 1885. He was a member of the Massachusetts Medical Society and the American Medical Association.

He is survived by his son, four grandchildren and three great-grandchildren.

RHEES — Morgan J. Rhees, M.D., of Waban, died August 25. He was in his forty-second year.

Dr. Rhees received his degree from Harvard Medical School in 1925. Formerly assistant director of the Massachusetts General Hospital, he was director of the Joseph H. Pratt Diagnostic Hospital. He was a member of the American, New England and Massachusetts Hospital Associations, and of the Massachusetts Medical Society.

His widow, his mother, two children and a sister and brother survive him.

RING — Barbara Taylor Ring, M.D., of Arlington, died August 31. She was in her seventieth year.

Born in Aberdeen, Scotland, Dr. Ring received her degree from Boston University School of Medicine in 1899. She was a member of the Somerville Medical Society, the American Academy of Physical Medicine and the New England Society of Physical Medicine. She was president of the board of trustees of the Ring Sanatorium, and was a fellow of the Massachusetts Medical Society and the American Medical Association.

She is survived by a son, a grandson, three brothers and three sisters.

TABOR — EDWARD O. TABOR, M.D., of Lowell, died August 25. He was in his sixty-sixth year.

Born in Hanover, New Hampshire, Dr. Tabor received his degree from Dartmouth Medical School in 1901. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and a son survive him.

CORRESPONDENCE

"ACCOUCHEMENTS FOR AMERICA"

To the Editor: Probably doctors know more about economics, politics and other nonmedical subjects than any other group of people, but I humbly beg to differ with the opinion of Dr. Francis H. Higgins on "bargains in babies," which appeared in the August 14 issue of the *Journal*. Our crackpot friends, Herr Hitler and Il Duce, have had similar ideas, but it is emphatically not what we need in this country.

Here is how the scheme would work out: the many intelligent, hard-working and patriotic young couples of the lower middle class would still have only one or two children; they would not feel that they could afford to take advantage of the bargain rates, because they do not have large enough incomes to provide for clothing, food and education for more children. But the people who do not know enough or care enough to limit the number of their children would be encouraged to have even more, if possible, because of the 25 per cent reduction for each succeeding baby. The final result would be an increase in the population, but with an increase in the proportion of those who are relatively unproductive and a corresponding decrease of able professional and technical people. Such a public would eventually welcome a totalitarian government, which would involve, among less important things, regimentation of the medical profession.

Why not put the medical economists to work figuring out some sort of subsidy or bargain rate for the many couples who would like to have more children and who would have more if they felt that they could provide decent living conditions for them? That would be a definitely patriotic step.

C. S. GREENWOOD
511 Center Street
Sheffield, Pennsylvania

BOOK REVIEWS

A Surgeon's Life: The autobiography of J. M. T. Finney. 8°, cloth, 396 pp. New York: G. P. Putnam's Sons, 1940. $3.50.

Finney, in his autobiography, covers an interesting period in the development of medicine in America. Trained in the best traditions of his time, at the Harvard Medical School and the Massachusetts General Hospital, he went to the Johns Hopkins Hospital when Welch, Osler, Halsted and Kelly were at their height. The seeds sown by these great pioneers had grown to fruit, and Finney, with his colleagues of the eighteen nineties, reaped a rich harvest. Little was added by the second generation, for it was a time of putting into practice the stimulation received from others, not for the development of new ideas. Many of Finney's contemporaries became good surgeons and fine physicians, but none, save Harvey Cushing, were of the genius type of their predecessors. This, in no way, detracts from the excellent work of Finney and his associates, for they did the best surgery in America of their day, and practiced the best medicine. Finney gives an intimate picture of life at Hopkins, but much of the picture lacks color and shading. The outlines are discernible, but no clear memory remains after reading his chapters, for the whole book lacks body and depth. A few stories help to enliven the drab narrative, and Finney's humor and infectious laughter are felt throughout. He always added a story to any group, and was often called on to relieve tense situations in hospital and overseas during World War I. He was the embodiment of sound common sense, the conciliator and the man of sound judgment. One would choose him, however, rather as a surgeon than as an author, and that is the choice, no doubt, that Finney would agree was the most fitting.

Diseases of the Digestive System. Edited by Sidney A. Portis, B.S., M.D. 8°, cloth, 952 pp., with 176 illustrations and 37 tables. Philadelphia: Lea and Febiger, 1941. $10.00.

This volume should prove to be an extremely useful text and reference book, for it has been carefully compiled by leading authorities. It presents a comprehensive and up-to-date study of gastroenterology. The material is well arranged in five parts, as follows: "Introduction," with chapters on history, anatomy, physiology and the interpretation of pain in the gastrointestinal tract; "Etiologic Factors," including parasites, neurogenic factors, gastrointestinal manifestations of other diseases, anemias of gastrointestinal origin, tuberculosis, allergy and the relation of the teeth and diet to gastrointestinal disease; "Diseases of the Esophagus, Stomach and Duodenum," with chapters on the esophagus, gastritis, peptic ulcer, alkalosis, cancer, benign tumors, syphilis, linitis plastica and duodenal ileus; "Other Diseases of the Digestive System," including affections of the liver, gall bladder, pancreas and small intestine, and regional ileitis and appendicitis; and "Diseases of the Large Bowel and Rectum," including chapters on functional disturbances, protozoal infections, bacillary dysentery, ulcerative colitis, mucous colitis, cancer, diverticulitis, melanosis, hemorrhoids and lymphopathia venereum.

The reviewer finds little to criticize. Modern methods of study, including gastroscopy and liver-function tests, receive a fair share of attention. Treatment is well considered in each chapter. Numerous references are given. Illustrations, tables and diagrams are very satisfactory. This book is highly recommended.

NOTICES

SEVENTH POSTGRADUATE SEMINAR IN NEUROPSYCHIATRY

The Metropolitan State Hospital, Waltham, recently announced the opening of the Seventh Postgraduate Seminar in Neuropsychiatry.

The course consists of three units: military neuropsychiatry, October 3 to 31; general psychiatry, November 3 to December 12; and general neurology, January 5 to April 10. It is open to a limited number of graduate physicians. The teaching staff comprises a number of recognized specialists in this field throughout the state, and is under the direction of Dr. Roy D. Halloran, superintendent, Metropolitan State Hospital, and Dr. Paul I. Yakovlev, clinical director, Walter E. Fernald State School.

FORUM ON ALLERGY

The fourth annual Forum on Allergy will be held in Detroit, Michigan, on January 10 and 11, 1942.